

#### Question Of the Day Archives:

**Monday, December 5, 2016**

##### Question:

Calcium oxalate is a widespread toxin found in many species of plants. What is the needle shaped crystal containing calcium oxalate called and what is the compilation of these structures known as?

##### Answer:

The needle shaped plant-based crystals containing calcium oxalate are known as raphides. A compilation of raphides forms the structure known as an idioblast. (Lim CS et al. Atlas of select poisonous plants and mushrooms. 2016 Disease-a-Month 62(3):37-66)

**Friday, December 2, 2016**

##### Question:

Which oral chelating agent has been reported to cause transient increases in plasma ALT activity in some patients as well as rare instances of mucocutaneous skin reactions?

##### Answer:

Orally administered dimercaptosuccinic acid (DMSA) has been reported to cause transient increases in ALT activity as well as rare instances of mucocutaneous skin reactions. (Bradberry S et al. Use of oral dimercaptosuccinic acid (succimer) in adult patients with inorganic lead poisoning. 2009 Q J Med 102:721-732)

**Thursday, December 1, 2016**

##### Question:

What is Clioquinol and why was it withdrawn from the market during the 1970s?

##### Answer:

According to the cited reference, "Between the 1950s and 1970s Clioquinol was used to treat and prevent intestinal parasitic disease [intestinal amebiasis]."

"In the early 1970s Clioquinol was withdrawn from the market as an oral agent due to an association with sub-acute myelo-optic neuropathy (SMON) in Japanese patients. SMON is a syndrome that involves sensory and motor disturbances in the lower limbs as well as visual changes that are due to symmetrical demyelination of the lateral and posterior funiculi of the spinal cord, optic nerve, and peripheral nerves. The majority of symptoms were reversible, but permanent disability has been reported in 1000 of the 10,000 total cases of SMON noted in Japan over the two decades the drug was in use." (Mao X and Schimmer AD. The toxicology of Clioquinol. 2008 Toxicology Letters 182:1-6)

**Wednesday, November 30, 2016**

##### Question:

A worker, who's job involves grinding magnets, is diagnosed with bilateral optic atrophy, retinopathy and bilateral nerve deafness. Which metal is the likely culprit?

##### Answer:

As described in the cited reference "Cobalt exerts well-known and documented toxic effects on the thyroid, heart and the hematopoietic system, in addition to the occupational lung disease, allergic manifestations and a probably carcinogenic action. Cobalt neurotoxicity is reported in isolated cases, and it has never been systematically treated. Bilateral optic atrophy and retinopathy, bilateral nerve deafness and sensory-motor polyneuropathy have been described long ago as a result of chronic occupational exposure to cobalt powder or during long-term treatment of anemia with cobalt chloride. (Catalani S et. al. Neurotoxicity of cobalt. 2012 Human Exp Tox 31(5): 421-437)

**Tuesday, November 29, 2016**

##### Question:

Prolonged alcohol use is the second most common cause for the development of acute pancreatitis (with the presence of gallstones being the most common cause for acute pancreatitis). What role does the type of alcohol ingested and/or the act of binge drinking of alcohol play in the development of acute pancreatitis?

##### Answer:

According to the cited reference "the type of alcohol ingested does not affect risk and binge drinking in the absence of long-term, heavy alcohol use does not appear to precipitate acute pancreatitis." (Forsmark CE et al. Acute pancreatitis. 2016 NEJM 375:1972-1981 and Phillip V et al. Incidence of acute pancreatitis does not increase during Oktoberfest, but is higher than previously described in Germany. 2011 Clin Gastroenterol Hepatol 9(11): 995-1000.e3)

**Monday, November 28, 2016**

##### Question:

"Megacolon", defined as dilatation of the colon greater than 6 cm in one or more colonic segments can be seen in individuals suffering from chronic spinal cord injury. What are the toxicologic/pharmacologic issues that may predispose to the development of megacolon in the face of chronic spinal cord injury?

##### Answer:

According to the cited reference, "Factors significantly associated with megacolon were older age, longer duration of injury, symptom of abdominal distension, radiological constipation, urinary outlet surgery, laxative use at least once weekly, use of anticholinergic drugs, and use of calcium-containing antacids.....Independent correlates of megacolon were more than 10 years elapsed since acute injury, age over 50 years, and use of > or = 4 laxative doses per month." (Harar D and Minaker KL. Megacolon in patients with chronic spinal cord injury. 2000 Spinal Cord 38:331-339)

**Friday, November 25, 2016**

##### Question:

Some have postulated a link between metal on metal joint arthroplasties and the development of a variety of cancers. What is the evidence for a causal link between cancer and metal on metal joint replacements?

##### Answer:

Credible evidence has not been developed to support the notion that metal on metal arthroplasties cause cancer. One study reported on 110,792 total hip and 29,800 total knee arthroplasties and found no causal link between cancer development and metal on metal arthroplasties. (Therani R et al. The risk of cancer following total hip or knee arthroplasty. 2001 J Bone Joint Surg (Am) 83-A: 774-780)

**Thursday, November 24, 2016**

##### Question:

Which areas of the brain are considered to be the primary brain regions involved in substance use disorders?

**Answer:**

According to the recently promulgated U.S. Surgeon General's Report on Alcohol, Drugs and Health (Facing Addiction in America), "...the key components of networks that are intimately involved in the development and persistence of substance use disorders are the basal ganglia, the extended amygdala and the prefrontal cortex. The basal ganglia control the rewarding or pleasurable, effects of substance use and are also responsible for the formation of habitual substance taking. The extended amygdala is involved in stress and the feelings of unease, anxiety, and irritability that typically accompany substance withdrawal. The prefrontal cortex is involved in executive function (i.e., the ability to organize thoughts and activities, prioritize tasks, manage time, and make decisions), including exerting control over substance taking. These brain areas and their associated networks are not solely involved in substance use disorders. Indeed, these systems are broadly integrated and serve many critical roles in helping humans and other animals survive. ( <https://addiction.surgeongeneral.gov/chapter-2-neurobiology.pdf>; accessed November 2016)

**Wednesday, November 23, 2016****Question:**

What factors are thought to exacerbate the development of QT prolongation in patients suffering from acute promyelocytic leukemia (APL) who are treated with arsenic trioxide?

**Answer:**

According to the cited reference "Because most of the patients receiving arsenic trioxide have been [previously] exposed to cardiotoxic chemotherapy [including all-trans retinoic acid and anthracycline based drugs], cardiac dysfunction is thought to be universal before arsenic trioxide therapy begins. In addition, hypokalemia and hypomagnesemia are among the most common arsenic trioxide-related side effects. Thus it has been proposed that QT prolongation and ventricular arrhythmias associated with arsenic could be exacerbated by concurrent electrolyte disturbances or previous chemotherapy-induced cardiac damage." (Drolet B et al. Unusual effects of a QT prolonging drug, arsenic trioxide on cardiac potassium currents. 2004 Circulation 109:26-29)

**Tuesday, November 22, 2016****Question:**

What is the most common cause of acquired nephrogenic diabetes insipidus? What is the current management for this problem?

**Answer:**

According to the cited reference, "The most common cause of acquired nephrogenic diabetes insipidus is long-term lithium treatment. The management of lithium-induced nephrogenic diabetes insipidus is challenging, even when the drug is discontinued and therapy is changed to thiazide diuretics, amiloride, and reduced sodium intake. Amiloride inhibits lithium entry into renal collecting-duct cells through the epithelial sodium channel. Thiazide diuretics and a low-sodium diet result in hypovolemia-induced activation of the renin-angiotensin-aldosterone which stimulates proximal tubule sodium and water resorption resulting in less volume delivery to the distal nephron." (Gordon CE et al. Acetazolamide in lithium-induced nephrogenic diabetes insipidus. 2016 NEJM 375:2008-2009 and Sands JM and Bichet DG. Nephrogenic diabetes insipidus. Ann Intern Med 2006;144:186-94)

**Monday, November 21, 2016****Question:**

What is Bismacine?

**Answer:**

According to the cited reference (dated July 2006) "FDA notified healthcare professionals and consumers not to use an injectable product called Bismacine, also known as Chromacine. Bismacine is not a pharmaceutical and has not been approved to treat any condition; however, it is being prescribed or administered by doctors of "alternative health" to treat Lyme disease.

This product contains high amounts of bismuth, a heavy metal that is used in some medications taken by mouth to treat Helicobacter pylori, a bacteria that can cause stomach ulcers. However, Bismacine is not approved in any form for use by injection. The FDA is investigating one report of a death and several reports of injury related to the administration of Bismacine. Individuals who believe they have suffered adverse events from receiving Bismacine should seek medical attention. Possible effects of bismuth poisoning include cardio-vascular collapse and kidney failure." ( <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm150503.htm>; accessed November

**Friday, November 18, 2016****Question:**

The U.S. Department of Health and Human Services released the 14th Report on Carcinogens (RoC) on November 3, 2016. The RoC is a congressionally mandated, science-based, public health document that NTP prepares for the [HHS Secretary](#). This cumulative report currently includes 248 listings of agents, substances, mixtures, and exposure circumstances that are known or reasonably anticipated to cause cancer in humans.

Five viruses, a chemical, and a metallic element are newly listed in latest Report. What are these new additions to the RoC in the 14th Report?

**Answer:**

The chemical trichloroethylene (TCE), and the metallic element cobalt and cobalt compounds that release cobalt ions in vivo, are being added to the list, as well as five viruses that have been linked to cancer in humans. The five viruses include human immunodeficiency virus type 1, human T-cell lymphotropic virus type 1, Epstein-Barr virus, Kaposi sarcoma-associated herpesvirus, and Merkel cell polyomavirus.

**Thursday, November 17, 2016****Question:**

What do Whitewater Arroyo, Marburg, Machupo and Lymphocytic Choriomeningitis viruses all have in common?

**Answer:**

These are viruses classified as "hemorrhagic fever" viruses and all cause Viral hemorrhagic fevers (VHF). Viral hemorrhagic fevers are illnesses characterized by fever and bleeding diathesis. Manifestations of VHF often include flushing of the face and chest, petechiae, frank bleeding, edema, hypotension, and shock. Malaise, myalgias, headache, vomiting, and diarrhea occur frequently. These are all agents of concern for possible terrorist release against populations. ( <https://webwiser.nlm.nih.gov/knownSubstanceSearch.do?groupBySelect=35>; accessed November 2016)

**Wednesday, November 16, 2016****Question:**

What is U-47700?

**Answer:**

According to the cited reference, "U-47700 is a novel synthetic opioid, and its abuse parallels that of heroin, prescription opioids, and other novel opioids. Law enforcement agencies report seizures of the drug in powder form and counterfeit tablets that mimic pharmaceutical opioids. Abuse of the drug often happens unknowingly to the user, and is encountered as a single substance as well as in combination with other drugs such as heroin and fentanyl. Some bags are marked with stamped logos, imitating a heroin sale. In addition, the drug can be pressed into pill format and marketed as a wide variety of prescription opioids. Because substances like U-47700 are often manufactured in illicit labs overseas, the identity, purity, and quantity are unknown, creating a "Russian Roulette" scenario for any user." ( <https://www.dea.gov/divisions/hq/2016/hq111016.shtml>; accessed November 2016)

**Tuesday, November 15, 2016****Question:**

A recent report indicated a large number of people exposed to broken metal halide lights developed keratoconjunctivitis. What is the mechanism for the development of this malady secondary to broken metal halide lights?

**Answer:**

According to the cited reference “Metal halide lamps produce an electric arc that travels through a mixture of mercury and metal halide gases, generating an intense white light. These lamps have a coated outer glass envelope surrounding the arc tube, which serves to filter out ultraviolet light. Metal halide lamps with a broken outer envelope emit ultraviolet radiation and pose a risk for Keratoconjunctivitis.” (Wagh V et al. Photokeratoconjunctivitis outbreak associated with damaged metal halide lamps- Maharashtra State, Western India, June 2016. MMWR Weekly / November 11, 2016 / 65(44): 1238–1239 and Food and Drug Administration. Ultraviolet radiation burns from high intensity metal halide and mercury vapor lighting remain a public health concern. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2014. <http://www.fda.gov/Radiation-EmittingProducts/RadiationSafety/AlertsandNotices/ucm116540.htm> accessed Oct 2016)

**Monday, November 14, 2016****Question:**

When individuals in the USA who are on methadone maintenance therapy are incarcerated, what typically happens with regard to their methadone therapy?

**Answer:**

According to the cited reference, “On incarceration in the USA, nearly 90% of people on prescribed methadone are forced to stop or taper off this treatment. This pervasive practice of summarily discontinuing an approved and effective therapy in correctional settings seems to be unique among medical treatments”. (Rich JD et al. Methadone continuation versus forced withdrawal on incarceration in a combined US prison and jail: a randomized open-label trial. 2015 Lancet 386:350-359)

**Friday, November 11, 2016****Question:**

What is the potential effect of the use of hydroxocobalamin on the measurement of carboxyhemoglobin?

**Answer:**

According to the cited reference, “Unfortunately, the red hue of hydroxocobalamin interferes with certain colorimetric laboratory analyses, rendering them inaccurate for variable time periods. Because hydroxocobalamin has a light-absorption peak at 532 nm, its presence may interfere with the use of CO-oximetry to measure carboxyhemoglobin (which has a light-absorption peak of 525 and 575 nm).” The cited Letter to the Editor describes two patients with “severe carbon monoxide poisoning and carboxyhemoglobin levels that were significantly falsely lowered after hydroxocobalamin therapy.” (Livshits Z et al. Falsely low carboxyhemoglobin level after hydroxocobalamin therapy. 2012 NEJM 367:1270-1271)

**Thursday, November 10, 2016****Question:**

Which form of mercury is of concern related to the breakage of compact fluorescent lamp (CFL) bulbs?

**Answer:**

Inhalational exposure to inorganic mercury vapor is of concern related to the breakage of compact fluorescent lamp (CFL) bulbs. Nance P. et. al. Human health risks from mercury exposure from broken compact fluorescent lamps (CFLs). 2012 Reg Tox Pharm 62(3):542-552

**Wednesday, November 9, 2016****Question:**

Ingestion of which mushroom species was responsible for a number of cases of delayed rhabdomyolysis in France during the late 1990's?

**Answer:**

Tricholoma equestre was reported to be the cause a number of cases of delayed rhabdomyolysis in France during the late 1990's. (Bedry R et al. Wild mushroom intoxication as a cause of rhabdomyolysis. 2001 NEJM 345 (11): 798-802)

**Tuesday, November 8, 2016****Question:**

Which chemical is known by the U.S. Department of Transportation as “Poison B”?

**Answer:**

According to the cited reference, “Phenol is designated as “Poison B” by the Department of Transportation (DOT), but no special containers are required due to its modest fire hazard and low reactivity.” ( <http://www.atsdr.cdc.gov/MHMI/mmgs115.pdf>; accessed November, 2016)

**Monday, November 7, 2016****Question:**

A recent report (see citation below) described “ocular flutter” as a rare manifestation of the serotonin syndrome. What is ocular flutter?

**Answer:**

“Nystagmus refers to eye movement abnormalities that are characterized by an abnormal slow phase followed by either a slow phase or a fast phase. Saccadic intrusions, on the other hand, are abnormal eye movements that have a pathologic fast saccade followed by a fast corrective saccade, with or without an intersaccadic interval. Ocular flutter, by contrast, is clinically characterized by intermittent bursts of conjugate, horizontal saccades without an intersaccadic interval.” (Kruger JM et al. Ocular flutter as the presenting sign of adenocarcinoma 2014 Digital J Ophthalmology and Sim SS and Sun JT. Ocular flutter in the serotonin syndrome. 2016 NEJM 375e38)

**Friday, November 4, 2016****Question:**

Which organ systems are affected by occupational exposure to the chemical epichlorohydrin?

**Answer:**

The cited reference reports: “In humans exposed to concentrations above 100 ppm for brief periods, lung edema and kidney lesions have been reported. Exposure at 20 ppm caused burning of eyes and nasal mucosa. Another exposure to an unknown concentration caused eye and throat irritation, nausea, dyspnea, bronchitis, and an enlarged liver. Painful irritation of subcutaneous tissues follows skin contact in humans.(<http://www.cdc.gov/niosh/pel88/106-89.html>; accessed October 2016)

**Thursday, November 3, 2016****Question:**

Dinitrotoluene (DNT) is a precursor chemical used in the production of the chemical toluene diisocyanate. Occupational exposure to DNT may result in what potentially life threatening hematologic toxicity?

**Answer:**

Exposure to DNT may cause methemoglobinemia. (<http://www.atsdr.cdc.gov/toxprofiles/tp109-c3.pdf>; accessed August 2016)

**Wednesday, November 2, 2016**

**Question:**

What is 1,3 butadiene?

**Answer:**

The cited reference notes: "1,3-Butadiene is a chemical made from the processing of petroleum. It is a colorless gas with a mild gasoline-like odor.

About 60% of the manufactured 1,3-butadiene is used to make synthetic rubber. Synthetic rubber is widely used for tires on cars and trucks. 1,3-Butadiene is also used to make plastics including acrylics. Small amounts are found in gasoline." This resource further points out "The Department of Health and Human Services (DHHS), IARC, and EPA have determined that 1,3-butadiene is a human carcinogen.

Studies have shown that workers exposed to 1,3-butadiene may have an increased risk of cancers of the stomach, blood, and lymphatic system. Animal studies found increases in a variety of tumor types from exposure to 1,3-butadiene. ( <http://www.atsdr.cdc.gov/toxfaqs/tf.asp?id=458&tid=81>; accessed October 2016)

**Tuesday, November 1, 2016**

**Question:**

What are photoallergic reactions?

**Answer:**

According to the cited reference, "Photoallergic reactions seem to be initiated by covalent binding of the photosensitizer to a skin protein, forming adducts capable of interacting with the immune system. The most frequent reactions of this type (photoallergic dermatitis) are induced by drugs and mediated by T cells. Diagnosis of photoallergy requires identification of the responsible agent, which is not always clear-cut. Photopatch testing is the method of choice for definitive diagnosis." (Andreu I et al. Generation of reactive intermediates in photoallergic dermatitis. 2010 Current Opinion in Allergy and Clinical Immunology 10:303–308)

**Monday, October 31, 2016**

**Question:**

Penicillins and cephalosporins (beta lactams) have been associated with the development of drug induced liver injury (DILI). What is the liver injury associated with the use of macrolide antibiotics?

**Answer:**

According to the cited reference, "Macrolides are generally associated with reversible cholestatic liver injury. The risk of erythromycin inducing DILI is estimated at 3.6/100,000 cases. Patients present with abdominal pain, anorexia, nausea and vomiting for 2–4 weeks following the initial administration or after 2–3 days if re-challenged, suggesting a hypersensitivity mechanism. Liver abnormalities generally subside within 2–5 weeks after stopping the drug. In rare cases, cholestasis persist for up to 6 months." (David S and Hamilton JP. Drug-induced liver injury. 2010 US Gastroenterol Hepatol Rev 6:73-80)

**Friday, October 28, 2016**

**Question:**

What is the role of the drug amifostine with regard to cisplatin related nephrotoxicity?

**Answer:**

The cited reference states "Amifostine (2-(3-aminopropylamino) ethylsulfanyl phosphonic acid) is approved by the U.S. Food and Drug Administration for use in reducing cumulative nephrotoxicity of repeated cisplatin dosing in patients with advanced ovarian cancer. Amifostine may derive its protective effects by providing a thiol group to normal versus malignant cells. Data are limited regarding the use in amifostine in tumors other than ovarian carcinoma." (Miller RP et al. Mechanisms of cisplatin nephrotoxicity. 2010 Toxins 2:2490-2518)

**Thursday, October 27, 2016**

**Question:**

How is isopropyl alcohol poisoning typically diagnosed?

**Answer:**

According to the cited reference, "Poisoning can be diagnosed using the measurement of isopropanol serum concentrations, though these may not be readily available. Diagnosis is therefore more typically made on the basis of the patient's history and clinical presentation. An osmol gap, ketonemia, and/or ketonuria without metabolic acidosis, along with a fruity or sweet odor on the breath and CNS depression support the diagnosis." (Slaughter RJ et al. Isopropanol poisoning. 2014 Clin Tox 52(5): 470-478)

**Wednesday, October 26, 2016**

**Question:**

What is dong quai and what effect does this substance have on blood clotting ability?

**Answer:**

According to the cited reference, dong quai, also known as Angelica polymorpha, is a Chinese herbal medication that has been recommended for "the treatment of menstrual cramping, irregular menses, and menopausal symptoms. Dong quai has a number of antithrombotic constituents, particularly coumarins, as well as constituents possessing antiarrhythmic effects." (McEwen BJ. The influence of herbal medicine on platelet function and coagulation: A narrative review. 2015 Semin Thromb Hemost 41:300-314)

**Tuesday, October 25, 2016**

**Question:**

"Coca cola colored babies" have been associated with pre-natal exposure to which group of chemicals?

**Answer:**

"Coca cola colored babies" have been associated with pre-natal exposure to chlorobiphenyls. (Miller RW. Coca cola colored babies". Chlorobiphenyl poisoning in Japan. 1971 Teratology. 4 (2): 211–212 and Reggiani G and Bruppacher R. Symptoms, signs and findings in humans exposed to PCBs and their derivatives. 1985 Env Health Persp 60:225-232)

**Monday, October 24, 2016**

**Question:**

Hepatocellular adenoma (HCA) is a benign tumor that may undergo malignant transformation and with a risk for spontaneous hemorrhage. Bleeding in HCA occurs in approximately 27.2 % of patients. Bleeding in hepatic adenomas has been associated with the use of which medications?

**Answer:**

Bleeding in hepatic adenomas, as well as increased tumor size, has been associated with the use of oral contraceptives. (Bieze M et al. Risk factors for bleeding in hepatocellular adenoma. 2014 Br J Surg 101:847-855)

**Friday, October 21, 2016**

**Question:**

Ischemic stroke is a reported phenomenon following hymenopteran sting albeit an extremely rare occurrence. Less than 20 cases have been published in the medical literature to date. What is the reported time range for the development of ischemic stroke following hymenopteran sting?

**Answer:**

According to the cited reference, the reported time range for the development of ischemic stroke following hymenopterian sting is less than 1 hour to as late as 24 hours following the sting. (Kulhari A et al. Ischemic stroke after wasp sting. 2016 J Emerg Med 51(4): 405-410)

**Thursday, October 20, 2016****Question:**

The use of intravenous lipid emulsion (ILE) therapy has gained increasing interest for the treatment of a variety of toxicities. A wide variety of adverse events have been reported in association with ILE therapy. What factors are associated with the development of adverse effects due to intravenous lipid emulsion therapy?

**Answer:**

According to the cited reference: "Both the rate of infusion and the total dose infused are associated with reactions to ILE. Guidelines for maximum doses and rates of infusion have been established for nutrition support and are based on reported adverse events such as dyspnea, cyanosis, flushing, hypercoagulability, hypertriglyceridemia and chest pain. In adults, infusion faster than the estimated maximum oxidation rate of 1.2–1.7 mg/kg/min (for ILE 20%, this is 0.35–0.51 mL/kg/h or 8.6–12.24 mL/kg/day) likely increases the risk of significant adverse events and is not recommended." Hayes BD et al Systematic review of clinical adverse events reported after acute intravenous lipid emulsion administration. 2016 Clin Tox 54(5): 365-404)

**Wednesday, October 19, 2016****Question:**

The population prevalence of latex allergy ranges from 3% to as high as 64%. In addition, as many as 20% of health care workers have been sensitized to latex. Which specific subset of patients are at special risk for latex sensitization?

**Answer:**

According to the cited reference, "Patients with spina bifida or urogenital abnormalities are a particular subpopulation at risk with a prevalence > 60% due to multiple surgeries early in life resulting in frequent exposure to latex." These individuals may also be exposed to latex resulting from life long urethral self-catheterization. (Kahn SL et al. Natural rubber latex allergy. 2016 Disease-a-Month 62(1):1-18)

**Tuesday, October 18, 2016****Question:**

What potentially life threatening effect has recently been posited by the combination of ceftriaxone with lansoprazole?

**Answer:**

The authors of the cited study report mining data from a robust database and discovering that: "Both direct and indirect signals in the adverse event reports provided evidence that the combination of ceftriaxone and lansoprazole will prolong the QT interval." They further report: "...patients taking both ceftriaxone and lansoprazole had significantly longer QTc intervals and were 1.4 times more likely to have a QTc interval above 500ms. In the laboratory we found that in combination and at clinically relevant concentrations, these drugs blocked the hERG channel." They also report "Class effect analysis suggested this interaction was specific to lansoprazole combined with ceftriaxone but not with other cephalosporins." (Lorberbaum T et al. Coupling data mining and laboratory experiments to discover drug interactions causing QT prolongation. 2016 J Am Coll Cardiol 68(16):1756-1764)

**Monday, October 17, 2016****Question:**

In 1955 a contamination incident involving the production of dry milk at the Morinaga Milk Company in Japan resulted in an outbreak of poisoning involving which chemical?

**Answer:**

The cited reference describes: "In the early summer of 1955, an outbreak of arsenic poisoning from ingestion of arsenic-contaminated milk powder occurred in western Japan. Arsenic contamination happened during the production of Morinaga Dry Milk at the Tokushima plant on Shikoku Island. The source of arsenic contamination was a disodium phosphate product added to cow's milk as a stabilizer to maintain constant acidity. This particular industrial-grade disodium phosphate product was of low purity and contained 5% to 8% arsenic (expressed as arsenious acid)." (Tanaka H et al. Long-term prospective study of 6104 survivors of arsenic poisoning during infancy due to contaminated milk powder in 1955. 2010 J Epidemiol 20(6): 439-445)

**Friday, October 14, 2016****Question:**

Tri-ortho-cresyl phosphate (TOCP) is an organophosphate compound that has been reported to cause a variety of adverse health effects in humans including neurotoxicity associated with the inhibition of both acetylcholinesterase and butyrylcholinesterase enzymes. Important historical episodes of TOCP toxicity associated with accidental (and intentional) food, beverage and drug contamination have been described. It is believed that a toxic metabolite of TOCP is causative of the neurotoxic effects. What is that metabolite?

**Answer:**

The cited reference reports cytochrome p-450 mediated bioactivation of TOCP to form the toxic metabolite 2-(ortho-cresyl)-4H-1,2,3-benzodioxaphosphoran-2-one (CBDP). These authors go on to note that "The formed CBDP can react with butyrylcholinesterase to form an organophosphorylated adduct, which undergoes two consecutive hydrolysis reactions which eventually leads to the formation of an ultimate phosphate adduct on the active site serine (Ser198)." (Reinen JJ. Characterization of human cytochrome P450s involved in the bioactivation of tri-ortho-cresyl phosphate (ToCP). 2015 Chem Res in Tox. 4: 711-721)

**Thursday, October 13, 2016****Question:**

What are so called "Data Monitoring Committees" (DMC)?

**Answer:**

DMC's are independent committees (also known as data and safety monitoring boards) established "to allow investigators and sponsors to manage [clinical] trials without bias, as well as to ensure an objective assessment of the accumulating data. According to the cited reference, these groups also "make recommendations regarding trial modifications, including early termination, to investigators and sponsors. These committees require multidisciplinary expertise and experience, including knowledge of statistical methods for interim data monitoring; they also pay attention to recruitment progress and the general quality of the trial with respect to adherence to the protocol and completeness of data collection and follow-up." (DeMets DL and Ellenberg SS. Data Monitoring Committees - Expect the unexpected. 2016 NEJM 375:1365-1371)

**Wednesday, October 12, 2016****Question:**

Allergic reactions to local anesthetics are not common however local anesthetics are indeed capable of causing potentially serious allergic reactions. What is the basis for the antigenicity of procaine and the ester local anesthetic agents that might cause allergic reactions?

**Answer:**

The antigenicity of procaine and the amino ester agents is "most often related to the para-aminobenzoic acid (PABA) component of ester anesthetics, a decidedly antigenic compound." PABA results from the metabolism of the ester agents. PABA does not form due to the metabolism of the amide agents. (Specia SJ et al. Allergic reactions to local anesthetic formulations. 2010 Dent Clin N Amer 54:655-664)

**Tuesday, October 11, 2016**

**Question:**

What is the ACGIH?

**Answer:**

The ACGIH is the “American Conference of Governmental Industrial Hygienists”. It is “a member-based organization that advances occupational and environmental health”. Originally convened as the “National Conference of Governmental Industrial Hygienists” in 1938, unlike OSHA and NIOSH, ACGIH is a non-governmental agency. “ACGIH is best known for its [Threshold Limit Values for Chemical Substances \(TLV®-CS\) Committee](#) established in 1941. This group was charged with investigating, recommending, and annually reviewing exposure limits for chemical substances. It became a standing committee in 1944. Two years later, the organization adopted its first list of 148 exposure limits, then referred to as Maximum Allowable Concentrations. The term “Threshold Limit Values (TLVs®)” was introduced in 1956. The first edition of [Documentation of the Threshold Limit Values](#) was published in 1962 and is now in its seventh edition. Today’s list of TLVs® includes over 700 chemical substances and physical agents, and more than 50 Biological Exposure Indices (BEIs®) for selected chemicals.” ([www.acgih.org](http://www.acgih.org); accessed October 2016)

**Monday, October 10, 2016**

**Question:**

What is the mechanism for bupivacaine induced lethal cardiac arrhythmias?

**Answer:**

According to the cited reference “Bupivacaine is a potent inhibitor of cardiac sodium channels, an interaction that contributed to its ability to induce lethal cardiac arrhythmias.” (Schwoerer AP et al. A comparative analysis of bupivacaine and ropivacaine effects on human cardiac SCN5A channels. 2015 Anesth Analg 120:1226-1234)

**Friday, October 7, 2016**

**Question:**

Bilobed lungs, malformed ears, coarctation of the aorta, situs inversus and epiphyseal stippling are common malformations are a consequence of maternal ingestion of which anticoagulant during pregnancy?

**Answer:**

Bilobed lungs, malformed ears, coarctation of the aorta, situs inversus and epiphyseal stippling are common malformations are a consequence of maternal ingestion of warfarin during pregnancy. (Mehdirattar S et al. Fetotoxicity of warfarin anticoagulation. 2010 Arch Gynecol Obstet 282:335-337)

**Thursday, October 6, 2016**

**Question:**

Dimethylacetamide (DMA) is used as a feedstock chemical in the resin and synthetic fiber industries. What is the target organ for this chemical when over exposure occurs and what is its general pathophysiology?

**Answer:**

According to the cited reference “The liver is the general target organ of N,N dimethylacetamide.” These authors go on to point out “The hepatic toxicity of DMA is well established in animals. Fatty infiltration of liver, increased liver weight, hepatic focal cystic degeneration, biliary hyperplasia, centrilobular single cell necrosis and elevated transaminase have been reported...”. In one reported human case, “A male worker in a synthetic elastic fibre factory who was exposed to mixed solvents including DMA in a confined space continuously for 4-6 hours per day for three days, developed hepatic injury with other clinical manifestations of acute DMA intoxication. Toxic hepatitis following excessive dermal exposure to DMA was reported among workers from a new acrylic fibre manufacturing line.” (Lee CY et al. Incidence of dimethylacetamide induced hepatic injury among new employees in a cohort of elastane fibre workers. 2006 Occup Environ Med 63:688-693)

**Wednesday, October 5, 2016**

**Question:**

Cases of lethality have been reported after acute inhalation exposure to a mixture of vapors of trimethyltin and dimethyltin organotin and after acute oral ingestion of trimethyltin. In 1954, approximately 100 deaths occurred in France following ingestion of a proprietary drug that seemed to have been contaminated with ethyltin triiodide, triethyltin iodide, or tetraethyltin. Deaths occurred after exposure to an estimate dose of 3 g triethyltin iodide over a period of 6–8 weeks. What symptoms were seen in these circumstances and may might be expected in other individuals exposed to organotin compounds including trimethyl and triethyl tins?

**Answer:**

According to the cited reference “Those affected showed neurological signs and symptoms such as headache, photophobia, altered consciousness, and convulsions. These appeared about 4 days after intoxication and, in individuals who recovered, continuous headaches and weakness persisted for at least 4 years. Additional cases of accidental or intentional acute inhalation, oral, or dermal intoxication with trimethyltin or triphenyltin also have included adverse neurological effects that persisted for a long time (years in some cases) after the poisoning episode. Organotins also are known to be skin and eye irritants in humans.” (ATSDR Toxicological Profiles for Tin and Tin Compounds. <http://www.atsdr.cdc.gov/toxprofiles/tp55-c2.pdf>; accessed September 2016)

**Tuesday, October 4, 2016**

**Question:**

Which non-selective herbicide, often used for vegetation control along roadsides, is characterized by the formation of methemoglobinemia, hemolysis, DIC and renal failure following ingestion?

**Answer:**

Sodium chlorate is the non-selective herbicide, often used for vegetation control along roadsides and is characterized by the formation of methemoglobinemia, hemolysis, DIC and renal failure following ingestion. With regard to the associated renal failure, the cited reference notes the “nephrotoxicity of chlorate is mediated by methemoglobinuria along with a vasoconstriction due to intravascular hemolysis that results in tubular damage. In addition, it must be considered a direct toxic effect on the proximal tubule of chlorate itself. Interestingly, sodium chlorate-dependent renal failure is characterized by the same histological lesions (fibrin deposition in afferent arterioles and glomerular capillaries) as those described in hemolytic uremic syndrome.” (Ranghino A et al. A case of acute sodium chlorate self-poisoning successfully treated without conventional therapy. 2006 Nephrol Dial Transplant 21:2971-2974)

**Monday, October 3, 2016**

**Question:**

What was “Koremu”?

**Answer:**

“Koremu” was a thallium acetate-containing, topically applied, depilatory used in the past (1920’s-1930’s). This now discontinued commercial product contained approximately 7% (or more) thallium acetate and was historically responsible for numerous cases of severe thallium intoxication including some deaths. (Severe thallium acetate intoxication caused by the use of a depilatory called “Koremu”. Rudy A. 1932 NEJM 207(25): 1151-1152)

**Friday, September 30, 2016**

**Question:**

Colchicine is used primarily to treat/prevent gout and to treat familial Mediterranean fever. What are the adverse effects of colchicine with regard to reproductive potential in both females and males?

**Answer:**

The cited reference notes: "Colchicine has not been shown to adversely affect reproductive potential in males or females. It crosses the placenta but there is no evidence of fetal toxicity. Colchicine is excreted into breast milk and considered compatible with lactation. (Finkelstein Y et al. Colchicine poisoning: the dark side of an ancient drug. 2010 Clin Tox 48(5): 407-414)

**Thursday, September 29, 2016**

**Question:**

What is the common name for the organism *Physalia physalis*? What is the primary toxin delivered by this organism and what is the mechanism of toxicity?

**Answer:**

*Physalia physalis* is commonly known as the Portuguese man-of-war. The cited reference points out "The main toxin of the man-of-war venom is a glycoprotein of 240 kDa which is called Physaliatoxin (potent cytotoxic and haemolytic toxicity), but numerous other components (enzymes, proteins) have been isolated from this venom. The mechanism of its neurotoxic and cardiotoxic action is still unclear." (Albadie M et al. Portuguese man-of war (*Physalia physalis*) envenomation on the Aquitaine coast of France: An emergency health risk. 2012 Clin Tox 50(7): 567-570)

**Wednesday, September 28, 2016**

**Question:**

What are the common side effects of lithium with regard to the thyroid?

**Answer:**

According to the cited reference "The common clinical side effects of the drug are goiter in up to 40% and hypothyroidism in about 20%. The most important clinically relevant action is the inhibition of thyroid hormone release". (Gupta Y et al. Development of Graves disease after long standing hypothyroidism on treatment, with acute toxicity to thionamides and lithium. 2012 BMJ Case Reports 2012(Jul31): 1-4)

**Tuesday, September 27, 2016**

**Question:**

What is the mechanism for the QT interval prolongation that can occur due to methadone and by what percent is the QTc generally increased following the initiation of methadone therapy?

**Answer:**

According to the cited reference, "Methadone as well as its derivative levacetylmethadol prolong the QT interval by inhibition of the rapid component of the delayed rectifier potassium ion current." One study cited by these authors reported "...an 8% increase of the QTc interval after initiation of methadone." (Sticherling C et al. Methadone-induced torsade de pointes tachycardias. 2015 Swiss Medical Weekly. 135(19-20):282-285)

**Monday, September 26, 2016**

**Question:**

Which human disease is caused by infection with the bacterium *Chlamydoiphila psittaci*? Which workers are at risk for this disease and what are the clinical manifestations?

**Answer:**

According to the cited reference, "psittacosis is a human disease caused by infection with the bacterium also causes avian chlamydiosis, a disease reported in psittacine birds such as parrots, cockatiels, and parakeets. *Chlamydoiphila psittaci* can be present in large numbers in the droppings of sick birds and in dust contaminated by infected droppings. The organism can remain infectious in the environment for months. Human infection usually occurs when a person inhales the bacterium shed in feces and secretions of infected birds." These authors also point out "Psittacosis is most commonly reported among people in close contact with domestic birds, such as bird owners, poultry farmers, veterinarians, and workers within pet shops and poultry-processing plants. ....Psittacosis has an incubation period of 1 to 4 weeks, and manifestations of disease can range from asymptomatic infection to systemic illness with severe pneumonia. Untreated psittacosis has a reported case-fatality rate of 15% to 20%." (Telfer BL et al. Probable psittacosis outbreak linked to wild birds. 2005 Emerg Inf Dis 11(3): 391-397)

**Friday, September 23, 2016**

**Question:**

Which drugs, often prescribed for osteoporosis, have been associated with an increased risk for inflammatory ocular adverse effects such as uveitis and scleritis?

**Answer:**

The bisphosphonates have been associated with an increased risk for inflammatory ocular adverse effects such as uveitis and scleritis. (Etminan M et al. Inflammatory ocular adverse events with the use of oral bisphosphonates: a retrospective cohort study. 2012 CMAJ 184(8): E431-E434)

**Thursday, September 22, 2016**

**Question:**

Which antiretroviral agent has been associated with severe hypersensitivity reactions sometimes leading to death?

**Answer:**

Abacavir has been associated with severe hypersensitivity reactions sometimes leading to death. (Cruciani M et al. Virological efficacy of abacavir: systematic review and meta-analysis. 2014 J Antimicrobial Chemo 69:3169-3180)

**Tuesday, September 20, 2016**

**Question:**

Exposure to benzyl alcohol in neonates (during the late 1907's and early 1980s) was responsible for the development of which named syndrome? What was the source for exposure to benzyl alcohol in the originally described cases of this syndrome in neonates? What was the most striking feature of this syndrome and what was the probable mechanism of injury?

**Answer:**

Exposure to benzyl alcohol in neonates was responsible for an out break of so-called "neonatal gasping syndrome". The cited article notes "They received multiple injections of heparinized bacteriostatic sodium chloride for flushing the catheters, and medications reconstituted with bacteriostatic water, both contained 0.9 percent benzyl alcohol." The most striking feature of this syndrome was "gasping and apnea" postulated to be related to "injury to the apneustic center of the brain stem located in the pons". It was further postulated that "benzyl alcohol or one of its metabolites may produce apnea and gasping by exerting direct toxic effects at these respiratory centers." (Gershanik J et al. The gasping syndrome and benzyl alcohol poisoning. 1982 NEJM 307(22): 1384-1388)



**Monday, September 19, 2016**

**Question:**

What is nabiximols?

**Answer:**

Nabiximols is an oromucosal spray that is absorbed buccally. It contains extracts from Cannabis sativa plants grown under license in the UK by the company GW Pharmaceuticals. These extracts contain 27 mg/ml THC and 25 mg/ml CBD per bottle, with trace amounts of other plant-derived cannabinoids and terpenoids. Each spray of nabiximols delivers 100 µL (2.7 mg THC and 2.5 mg CBD) doses. Buccal administration provides a more rapid onset of action and more favorable pharmacokinetics than oral THC. Nabiximols is available in 15 countries for symptomatic relief of spasticity in multiple sclerosis and is in development for cancer-related pain.

The THC component of nabiximols provides the agonist substitution and the buccal route of administration gives relatively low and steady plasma THC concentrations relative to the large spikes observed with smoked or vaporized cannabis. The CBD content of nabiximols is potentially a major innovation over other CB1 receptor agonists such as dronabinol and nabilone, although direct comparisons for cannabis dependence have not been carried out yet." Nabiximols is not currently licensed in the United States.(Allsop DJ et al. Cannabinoid replacement therapy (CRT): nabiximols (Sativex) as a novel treatment for cannabis withdrawal. 2015 Clin Pharm Ther 97(6): 571-574)

**Friday, September 16, 2016**

**Question:**

What is the usual pattern of pain associated with brown recluse spider bites?

**Answer:**

Pain associated with a brown recluse spider bite usually begins at low, relatively tolerable levels and increases in intensity over the first 24 hours to levels often characterized as "severe". According to the cited reference, this pain pattern is consistent with a so-called "cytokine pain pattern with inflammation". However these authors also point out that "besides cytokine release, brown recluse spider venom may cause pain via other peripheral pathways, including direct action on peripheral nerve transport analogous to that of tetanus toxin" (Payne KS et al. Extreme pain from brown recluse spider bites- Model for cytokine driven pain. 2014 JAMA Dermatol 150(11): 1205-1208)

**Thursday, September 15, 2016**

**Question:**

What is the toxin contained in the seeds of the so-called Pong-Pong or "suicide" tree?

**Answer:**

Cerberin is the toxin contained in the seeds of the so-called Pong-Pong or "suicide" tree. This toxin is reported to cause classic cardiac glycoside toxicity.(Gaillard Y et al. Cerbera odollam: a "suicide tree" and cause of death in the state of Kerala, India. 2004 J Ethnopharm 95:123-126 and Wermuth M et al. Two deaths from intentional ingestion of non-native Pong-Pong tree (Cerebra odollam) seeds. Poster presentation at NACCT 2016, Boston, MA)

**Wednesday, September 14, 2016**

**Question:**

Which drug is sometimes referred to as "poor man's" methadone?

**Answer:**

Loperamide has been referred to by some as the "poor man's methadone". The cited study "suggests that loperamide is being used extra-medically to self-treat opioid withdrawal symptoms. There is a growing demand among people who are opioid dependent for drugs to control withdrawal symptoms, and loperamide appears to fit that role. The study also highlights the potential of the Web as a "leading edge" data source in identifying emerging drug use practices." (Daniulaityte R. "I just wanted to tell you that loperamide WILL WORK": A web-based study of extra-medical use of loperamide. 2013 Drug and Alcohol Dependence 130: 241-244)

**Tuesday, September 13, 2016**

**Question:**

What is microcystin toxin?

**Answer:**

Microcystin is a hepatotoxin released by cyanobacteria in certain harmful algal blooms. Exposure to microcystin has been associated with gastrointestinal and hepatic illness in both humans and animals. (McCarty CL et al. Community Needs Assessment After Microcystin Toxin Contamination of a Municipal Water Supply — Lucas County, Ohio, September 2014. MMWR September 9, 2016, 65(35): 925-929)

**Monday, September 12, 2016**

**Question:**

One commonly referenced model of chemical carcinogenesis involves three stages: initiation, promotion and progression. What is the distinction between these three stages?

**Answer:**

According to the cited reference: "We define tumor initiators as carcinogens capable to induce a first driver mutation in a dividing cell, through direct or indirect mutagenesis, so that an initial clone of mutated cells can emerge. We define tumor promoters as non-genotoxic carcinogens capable to cause clonal expansion of initiated cells, i.e. able to induce proliferation of mutated cells and to prevent these cells from apoptotic loss, so the possibility of additional genetic and/or epigenetic changes is preserved. We define tumor progressors as carcinogens that advance mutated cells from promotion to progression, i.e. that allow premalignant mutated cells to irreversibly acquire the phenotype of fully malignant cells. (Irigaray P and Belpomme D. Basic properties and molecular mechanisms of exogenous chemical carcinogens. 2010 Carcinogenesis, 31(2): 135-148)

**Friday, September 9, 2016**

**Question:**

What is the distinction between carcinogens and cocarcinogens?

**Answer:**

According to the cited reference: "By definition, carcinogens are cancer-causing agents, whereas cocarcinogens are not carcinogenic agents, rather agents that can activate carcinogens and/or enhance their carcinogenic effects. Accordingly, xenochemicals such as PAHs, NOCs, AAs, HAAs and PHAHs such as dioxins, PCBs and organochlorine pesticides are exogenous carcinogens, whereas chemicals that deplete the organism of endogenous detoxifying proteins such as glutathione (GSH), that inhibit phase I and/or phase II xenobiotic metabolizing enzymes, that loosely couple the detoxifying effects of phase I oxidative enzymes and of phase II-conjugating enzymes, that inhibit DNA repair enzymes or conversely that activate procarcinogens into carcinogens through induction of the CYP system are all cocarcinogens." (Irigaray P and Belpomme D. Basic properties and molecular mechanisms of exogenous chemical carcinogens. 2010 Carcinogenesis 31(2): 135-148)

**Thursday, September 8, 2016**



**Question:**

Benzidine and beta-naphthylamine are known carcinogens for which organ?

**Answer:**

Benzidine and beta-naphthylamine are known bladder carcinogens. (ATSDR. Addendum to the Toxicological Profile for Benzidine. September 2009)

**Wednesday, September 7, 2016****Question:**

What characterizes so-called baker's asthma?

**Answer:**

According to the cited reference: "Baker's asthma is one of the most common causes of occupational asthma, and annual incidence of disease ranges between one and 10 cases per 1000 bakery workers. Any worker who is exposed to bakery allergens can develop the disease (including confectioners, flour miller and food processors), not only bakers. The main agents that cause baker's asthma are cereal flours (wheat, rye and barley) and enzymes, but new allergens are being used. Baker's asthma is mediated through the classical IgE allergic pathway, and accurate measurement of sensitization to bakery allergens is essential for diagnosis." The authors of the cited reference note: "A new family of cereal allergens has been identified, including wheat thioredoxin hb (Tri a25). New enzymes are being added to bread that may have allergic potential. The relationship of specific sensitization and baker's asthma has been confirmed in further studies." (Brant A. Baker's asthma. 2007 Curr Opin Allergy Clin Immunol 7:152-155)

**Tuesday, September 6, 2016****Question:**

What is the standard reference for information regarding drug induced torsades de pointes and drugs that induce prolongation of the QT?

**Answer:**

The standard reference for information regarding drug induced torsades de pointes and drugs that induce prolongation of the QT is the website [www.crediblemeds.org](http://www.crediblemeds.org).

CredibleMeds® was founded in 1999 as the university-based, federally funded Center for Education and Research on Therapeutics (CERT), with a mission to foster the safe use of medicines. In 2012, CERT became AZCERT or Arizona CERT, an independent non-profit 501c3 organization incorporated in Arizona. AZCERT's website was renamed CredibleMeds® in 2014 to better reflect its scope and global recognition as a trusted resource on safe medication use for healthcare providers, research scientists and the public. AZCERT maintains the CredibleMeds® website and the QTdrugs lists of drugs that have a risk of QT prolongation and cardiac arrhythmias under a contract with the FDA's Safe Use Initiative to support the safe use of medications.

Since its initial launch in 1999, CredibleMeds® has developed educational and research programs providing resources for medical professionals, researchers and consumers. Most notably, CredibleMeds® has built and applied a novel, systems-based approach to reduce harm from medications and drug-drug interactions (DDIs) – with a special focus on drugs that prolong the QT interval on the patient's electrocardiogram and thereby increase the risk of torsades de pointes (TdP), a heart arrhythmia that can cause sudden cardiac death. ([www.crediblemeds.org](http://www.crediblemeds.org); accessed Sept 2016)

**Monday, September 5, 2016****Question:**

Question of the Day will resume tomorrow.

Happy Labor Day to all!!

**Answer:**

Question of the Day will resume tomorrow.

Happy Labor Day to all!

**Friday, September 2, 2016****Question:**

What is the so-called "pine mouth syndrome" (PMS)?

**Answer:**

The "pine mouth syndrome" is also known as the "pine nut syndrome" and is reportedly associated with the ingestion of pine nuts. Possible etiologies included ingestion of rancid nuts, unknown toxins / fungi, or possible adulterants.

According to the cited article "A clinically compatible case of PMS must include a complaint of a taste disturbance, usually characterized as bitter or metallic. This taste disturbance must follow the ingestion of affected pine nuts, usually by 1 to 3 days. Affected nuts would appear to include all, or some portion, of nuts harvested from species *Pinus armandii*, but could include nuts from other species. The taste disturbance must resolve (without treatment) within one month, and usually within 1 to 2 weeks. Patients must not present with any other related neurologic deficits except for mild headache. Patients should have no other obvious explanation for cogeusia or metallogueusia, such as the recent ingestion of medications known to cause these symptoms." (Munk MD. Pine mouth (pine nut) syndrome: description of the toxidrome, preliminary case definition, and best evidence regarding an apparent etiology. 2012 Sem in Neurol 32(5): 525-527)

**Thursday, September 1, 2016****Question:**

Which recently enacted federal law directs federal agencies to provide recommendations for the diagnosis and treatment of infants undergoing neonatal abstinence syndrome (NAS)?

**Answer:**

The Protecting Our Infants Act of 2015 directs federal agencies to provide recommendations for the diagnosis and treatment of infants undergoing neonatal abstinence syndrome (NAS). (Kaltenbach K and Jones HE. Neonatal abstinence syndrome: Presentation and treatment considerations. 2016 J Addict Med 10(4): 217-223)

**Wednesday, August 31, 2016****Question:**

What is diazinon and what is the urinary metabolite biomarker unique to this chemical?

**Answer:**

Diazinon is the common name of an organophosphorus pesticide used to control pest insects in soil, on ornamental plants, and on fruit and vegetable field crops. It was formerly used as the active ingredient in household and garden products used to control pests such as flies, fleas, and cockroaches.

Diazinon is a synthetic chemical, it does not occur naturally in the environment. Pure diazinon is colorless and practically odorless oil. Preparations used in agriculture and by exterminators contain 85-90% diazinon and appear as a pale to dark-brown liquid. Diazinon preparations sold in the past for home and garden use contained 1-5% diazinon in a liquid or as solid granules. Most diazinon used is in liquid form, but it is possible to be exposed to the solid form. Diazinon does not dissolve easily in water and does not burn easily.

Biomarkers of recent exposure to diazinon may include plasma and rbc cholinesterase activity levels and urinary levels of metabolites IMHP, DETP, and DEP; only IMHP (2-isopropyl-4-methyl-6-hydroxy- pyrimidine) is unique to diazinon. ( <http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=90>; accessed August 2016)

**Tuesday, August 30, 2016**

**Question:**

Germander is an aromatic plant in the mint family. Herbal teas prepared from this plant have been used for a variety of purposes including as an “antipyretic, diuretic, choleric and for abdominal disorders and wounds”. What is the primary toxicity associated with germander ingestion and what is the proposed mechanism?

**Answer:**

The primary toxicity associated with the ingestion of germander is liver toxicity. According to the cited reference, Germander related hepatotoxicity is “mediated via its furano neoclerodane diterpenoids, mainly teucriin A. Activation of the furano ring by cytochrome P450 3A results in the formation of toxic reactive epoxides. It is likely that Germander-induced hepatitis may be due to both direct toxicity and secondary immune reactions, probably with a varying contribution of these two mechanisms in different patients”. (Goksu E et al. Hepatitis: a herbal remedy Germander. 2012 Clin Tox 50: 158)

**Monday, August 29, 2016**

**Question:**

With regard to the current epidemic of street drugs, what does the abbreviation “IMF” stand for?

**Answer:**

The cited reference notes: “IMF” is “illegally manufactured fentanyl”, obtained through illicit drug markets, includes fentanyl analogs, and is commonly mixed with or sold as heroin. Starting in 2013, the production and distribution of IMF increased to unprecedented levels, fueled by increases in the global supply, processing, and distribution of fentanyl and fentanyl-precursor chemicals by criminal organizations.” (Gladden RM et al. Fentanyl law enforcement submissions and increases in synthetic opioid-involved overdose deaths — 27 States, 2013–2014. August 26, 2016 MMWR 65(33): 837-

**Friday, August 26, 2016**

**Question:**

What are the proposed mechanisms for acyclovir induced nephrotoxicity?

**Answer:**

The cited reference states: “For decades, acyclovir-induced nephrotoxicity was believed to be secondary to crystalluria. Clinical evidence of nephrotoxicity in the absence of crystalluria suggests that acyclovir induces direct insult to renal tubular cells. We postulated that acyclovir is metabolized by the alcohol dehydrogenase (ADH) enzyme to acyclovir aldehyde, which is metabolized by the aldehyde dehydrogenase 2 (ALDH2) enzyme to 9-carboxymethoxymethylguanine (CMMG). We hypothesized that acyclovir aldehyde plays a role in acyclovir-induced nephrotoxicity.” (Gunness P et al. Acyclovir-induced nephrotoxicity: the role of the acyclovir aldehyde metabolite. 2011 Trans Research 158:290-301)

**Thursday, August 25, 2016**

**Question:**

The reference cited below notes “Scombroid poisoning occurs after the ingestion of fresh, canned or smoked fish with high histamine levels due to improper processing or storage.” What are the effects of high levels of histamine in fish meat with regard to appearance, taste and smell of the fish?

**Answer:**

The cited reference states “ Scombroid poisoning is frequently misdiagnosed. Because histamine does not alter the organoleptic quality, the fish may seem normal. However, elevate histamine levels can occur in fish owing to improper refrigeration before processing or to storage of the fish at room temperature after cooking. Therefore, the appearance, taste and smell of the fish are poor guides as to the presence of histamine.” (Stratta P and Badino G. Five things to know about Scombroid poisoning. 2012 CMAJ 184(6): 674)

**Wednesday, August 24, 2016**

**Question:**

High dose treatment with which water soluble vitamin may cause laboratory abnormalities indistinguishable from those of Graves’ disease?

**Answer:**

According to the cited reference, “...biotin may interfere with the most commonly used thyrotropin and thyroid hormone assays. The results [were] falsely increased or decreased according to whether a competitive method of measurement (for free T4 and total T3) or non competitive method (for thyrotropin) was used. In addition, biotin also interfered in a competitive manner with the method used for detection of anti-thyrotropin receptor antibodies. Together threshold effects resulted in a laboratory pattern indistinguishable from that of Graves’ disease.” (Kummer S et al. Biotin treatment mimicking Graves’ disease. 2016 NEJM [correspondence] 375: 704-706)

**Tuesday, August 23, 2016**

**Question:**

What is benzo[a]pyrene? How does exposure to this chemical occur? What are the potential health consequences associated with medically important exposures to this chemical?

**Answer:**

Benzo[a]pyrene B[a]P is a five-ring polycyclic aromatic hydrocarbon (PAH). The cited reference notes “PAHs are ubiquitous environmental pollutants and emitted into surrounding environment (i.e., air, soil, water, etc.) via incomplete combustion of coal, oil, gas, wood, other carbon-containing organic materials and/or cigarette smoke. These ultimately result in human (or other organism, e.g., wildlife) exposure through direct (water, diet) or indirect (dust, air) routes.” These authors further note: “B[a]P is the prototypical PAH and categorized as a pro-carcinogen. The tumorigenic effects of B[a]P are likely mediated via metabolic activation by cytochrome P450 enzymes and epoxide hydrolase into the highly reactive electrophilic metabolite, BPDE; this ultimately forms adducts through covalent binding to DNA and/or albumin. PAH-albumin adducts have been used as a sensitive indicator of chronic low-level PAH exposure, due to lack of repair mechanisms for albumin as compared to DNA.” Some B[a]P exposures have been linked to cancer in a variety of organs including liver and lung. (Tian M et al. Association of environmental benzo[a]pyrene exposure and DNA methylation alterations in hepatocellular carcinoma: A Chinese case– control study. 2016 Sci Total Env 541:1243-1252)

**Monday, August 22, 2016**

**Question:**

One week to several months after tattooing of human skin "benign nodules, warts, plaques or ulcerated lesions" may develop primarily within areas of the tattoo containing red pigment. What are these lesions called?

**Answer:**

The benign nodules, warts, plaques or ulcerated lesions that may develop within areas of tattoos with red pigment are termed pseudoepitheliomatous hyperplasia. (Piccinini P et al. safety of tattoos and permanent make-up. Final report. 2016 European Commission JRC Science for Policy Report. EUR 27947 EN; doi: 10.2788/011817

**Friday, August 19, 2016**

**Question:**

What is isophorone? What is its characteristic odor and what are the industrial uses of this chemical?

**Answer:**

Isophorone is a clear liquid that smells like peppermint. It can be dissolved in water and evaporates somewhat faster than water. It is an industrial chemical used as a solvent in some printing inks, paints, lacquers, and adhesives. It is also used as an intermediate in the production of certain chemicals. Although isophorone is an industrial chemical, it also occurs naturally in cranberries. (<http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=148>; accessed July 2016)

**Thursday, August 18, 2016**

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**Question:**

What is the association between frequent acetaminophen use and asthma related complications in children?

**Answer:**

A recent multicenter, prospective, randomized, double-blind, parallel-group trial involving 300 children (age range 12-59 months) concluded "Among young children with mild persistent asthma, as-needed use of acetaminophen was not shown to be associated with a higher incidence of asthma exacerbations..." (Sheehan WJ et al Acetaminophen versus ibuprofen in young children with mild persistent asthma. 2016 NEJM 375: 619-630)

**Wednesday, August 17, 2016**

**Question:**

Clomiphene citrate (CC) has been used as a first line drug for the treatment of subfertility. Which birth defects have been associated with the use of clomiphene citrate?

**Answer:**

According to the cited reference, CC use was reported by 1.4% of control mothers (94/6500). Among 36 case-groups assessed, increased adjusted odds ratios (aOR) were found [all: aOR, 95% confidence interval (CI)] for anencephaly (2.3, 1.1-4.7), Dandy-Walker malformation (4.4, 1.7-11.6), septal heart defects (1.6, 1.1-2.2), muscular ventricular septal defect (4.9, 1.4-16.8), coarctation of aorta (1.8, 1.1-3.0), esophageal atresia (2.3, 1.3-4.0), cloacal extrophy (5.4, 1.6-19.3), craniosynostosis (1.9, 1.2-3.0) and omphalocele (2.2, 1.1-4.5)." These authors concluded: "Several associations between CC use and birth defects were observed. However, because of the small number of cases, inconsistency of some findings with previous reports, and the fact that we cannot assess the CC effect separately from that of the subfertility, these associations should be interpreted cautiously." (Reefhuis J et al. Use of clomiphene citrate and birth defects, National Birth Defects Prevention Study, 1997-2005) 2010 Human Repro 26(2): 451-457)

**Tuesday, August 16, 2016**

**Question:**

Various enzymes may act as sensitizers in the setting of occupational asthma. Workers in which industries may be exposed to enzymes and thus enzyme-induced occupational asthma?

**Answer:**

Some laboratory workers, pharmaceutical workers, and bakery workers may be exposed to enzymes and thus may be at risk for the development of enzyme-induced occupational asthma. (Tarlo SM and Lemiere C. Occupational Asthma 2014 NEJM 370:640-649)

**Monday, August 15, 2016**

**Question:**

Recombinant G-CSF is widely used for neutrophil recovery after chemotherapy, bone marrow/peripheral stem cell transplantation and in the management of neutropenia due to other causes including AIDS and certain hematologic problems involving deficient granulocyte production. What are the most common adverse effects associated with the use of G-CSF and what are the potentially life-threatening complications of this therapy?

**Answer:**

According to the cited reference, "The most common adverse events are bone pain (84%), headache (80%) and fatigue. Life-threatening complications such as stroke, myocardial infarction and splenic rupture, resulting from short-term or long-term use of these agents, however rare, can occur." (Akyol G et al. A rare but severe complication of filgrastim in a healthy donor: Splenic rupture. 2014 Transfusion Apheresis Sci 50:53-55)

**Friday, August 12, 2016**

**Question:**

What are the clinical manifestations of so-called Ackee fruit toxicity?

**Answer:**

According to the cited reference: "Ackee fruit toxicity has been known since the nineteenth century and popularly called "Jamaican vomiting sickness" because of the characteristic severe bouts of vomiting. Toxicity is dose dependent and usually manifests within 6-48 hours of ingestion with recovery usually within 1 week. Symptoms begin with intense vomiting, followed by a quiescent phase and then subsequently more vomiting, seizures, and coma. In fatal cases, death usually occurs within 48 hours of ingestion. Hypoglycemia, hepatic injury, and aciduria have been found to accompany the clinical manifestations." (Katibi OS, et al. Case Report: Ackee fruit poisoning in eight siblings: Implications for public health awareness. 2015 Am. J. Trop. Med. Hyg., 93(5): 1122-1123)

**Thursday, August 11, 2016**

**Question:**

What is "Refined Oil of Nepeta cataria" and what is it used for?

**Answer:**

The active ingredient found in "Refined oil of Nepeta cataria" is a multi-component extract of oil Nepeta cataria which is a member of the mint family of plants (Labiatae). The technical grade active ingredient (TGAi) is identified as Refined Oil of Nepeta cataria and is also referred to as Hydrogenated Catmint Oil (HCO). The technical grade active ingredient is intended for use in the manufacture of a dermally applied insect repellent for direct application to human skin to repel black flies, mosquitoes and other biting insects.

( [https://www3.epa.gov/pesticides/chem\\_search/reg\\_actions/registration/decision\\_PC-004801\\_25-Aug-10.pdf](https://www3.epa.gov/pesticides/chem_search/reg_actions/registration/decision_PC-004801_25-Aug-10.pdf); accessed August 2016)

**Wednesday, August 10, 2016**

**Question:**

What are sulfur mustard agents H/HD and HT and how do they differ from each other?

**Answer:**

The cited reference reports: "Sulfur mustards H/HD and HT are manufactured compounds. They are colorless when pure, but are typically yellow to brown oily liquids with a slight garlic or mustard odor. Agent H contains about 20-30% impurities. The nearly pure substance is called HD. HT is a mixture of 60% HD and 40% of another substance called agent T. They do not dissolve much in water, but dissolve easily in oils, fats, and other solvents. They are stable at ambient temperatures.

Sulfur mustards were introduced as chemical warfare agents during World War I. More than a dozen countries have sulfur mustard agents in their chemical arsenals. Destruction of U.S. stockpiles of chemical agents, including sulfur mustards, was mandated by the Chemical Weapons Convention to take place before April 2007."

( <http://www.atsdr.cdc.gov/toxfaqs/TF.asp?id=926&tid=191>; accessed July 2016)

**Tuesday, August 9, 2016**

**Question:**

Recent reports indicate an increase in cyclospora-related illness in humans. Ingestion of which foods have been associated with US outbreaks of cyclospora-related illness over the past decade?

**Answer:**

Ingestion of imported fresh produce, including fresh cilantro, pre-packaged salad mix, raspberries, strawberries, basil, snow peas and mesclun lettuce have been involved in US outbreaks of cyclospora-related illness over the past decade. (Vignes-Kendrick et al. Outbreaks of cyclosporiasis- United States, June- August 2013. MMWR 62(43): 862)

**Monday, August 8, 2016**

**Question:**

What chemical, marketed as a veterinary sedative analgesic (also as an antiemetic in cats), has been noted as an adulterant in heroin and other drugs of abuse and has been associated with central nervous system depression, respiratory depression, bradycardia, hypotension, and death in humans?

**Answer:**

Xylazine is a drug marketed as a veterinary sedative analgesic (also as an antiemetic in cats), has been noted as an adulterant in heroin and other drugs of abuse and has been associated with central nervous system depression, respiratory depression, bradycardia, hypotension, and death in humans. Interestingly, xylazine has a tricyclic structure similar to the tricyclic antidepressants. (Ruiz-Colon K et al. Xylazine intoxication in humans and its importance as an emerging adulterant in abused drugs: A comprehensive review of the literature. 2014 For Sci Int 240: 1-8)

**Friday, August 5, 2016**

**Question:**

What is a phase I clinical trial?

**Answer:**

A phase I clinical trial involves researchers testing a new drug or treatment in a small group of people for the first time to evaluate its safety, determine a safe dosage range and identify side effects. ( <https://www.nlm.nih.gov/services/ctphases.html>; accessed July 2016)

**Thursday, August 4, 2016**

**Question:**

SGLT2 inhibitors may predispose some diabetic patients to the development of ketoacidosis. Patients with which form of diabetes (type I or Type II) are subject to this risk?

**Answer:**

The cited reference points out that SGLT2 inhibitors may increase the risk of ketoacidosis in patients with both type I and Type II diabetes. (Taylor SI et al. SGLT2 inhibitors may predispose to ketoacidosis. 2015 J Clin Endocrinol Metab 100(8): 2849-2852)

**Wednesday, August 3, 2016**

**Question:**

What is the EPA definition of acute reference dose?

**Answer:**

The EPA definition of acute reference dose is “An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure for an acute duration (24 hours or less) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's non-cancer health assessments.” ( [https://ofmpub.epa.gov/sor\\_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do?details=&glossaryName=IRIS%20Glossary](https://ofmpub.epa.gov/sor_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do?details=&glossaryName=IRIS%20Glossary); accessed July 2016)

**Tuesday, August 2, 2016**

**Question:**

Vitamin D toxicity is an uncommon occurrence in children and adolescents. What characterizes these cases when they do occur?

**Answer:**

According to the cited reference, “Recent cases of intoxication relate to errors in manufacturing, formulation, or prescription; involve high total intake in the range of 240 000 to 4 500 000 IU; and present with severe hypercalcemia, hypercalciuria, or nephrocalcinosis. However, mild hypercalcemia and hypervitaminosis using currently recommended doses have been reported in infants with rickets.” These authors concluded: “Although rare, cases of vitamin D intoxication that present with dramatic life-threatening symptoms still occur in children. Moreover, recent studies in infants raise a potential need for monitoring vitamin D levels when doses at or above the currently recommended upper range are used. Further studies are needed to clarify these findings. The Drugs and Therapeutics Committee of the Pediatric Endocrine Society suggests obtaining serum 25-hydroxyvitamin D levels in infants and children who receive long-term vitamin D supplementation at or above the upper level intake that is currently recommended.” (Vogiatzi MG et al. Vitamin D supplementation and risk of toxicity in pediatrics: A review of current literature. 2014 J Clin Endocrinol Metab 99:1132-1141)

**Monday, August 1, 2016**

**Question:**

Which plant, consumed throughout the world for its stimulant effects and as an opioid substitute, is typically brewed into a tea, chewed, smoked or ingested in capsules and is also known as Thang, Kakuam, Thom, Ketum and Biak?

**Answer:**

Kratom (*Mitragyna speciosa*) is consumed throughout the world for its stimulant effects and as an opioid substitute, is typically brewed into a tea, chewed, smoked or ingested in capsules and is also known as Thang, Kakuam, Thom, Ketum and Biak. Some published case reports have associated kratom exposure with psychosis, seizures and death. (Anwar M et al. Notes from the Field: Kratom (*Mitragyna speciosa*) Exposures Reported to Poison Centers — United States, 2010–2015. MMWR July 29, 2016, 65(29):748-749)

**Friday, July 29, 2016**

**Question:**

The PRES syndrome (posterior reversible encephalopathy syndrome) has been reported in association with a wide variety of conditions including eclampsia, post organ transplant, neoplasia and chemotherapy treatments, systemic infections and kidney disease among others. Which venomous insect/arachnid stings have been reported to be associated with the development of PRES?

**Answer:**

In rare instances, wasp stings and scorpion stings have been reported to be associated with the development of PRES. (Marrone LCP et al. Posterior reversible encephalopathy syndrome following a scorpion sting. 2013 J Neuroimaging 23(4): 535-536)

**Thursday, July 28, 2016**

**Question:**

What is phytophotodermatitis? Exposure to which plants are the most common culprits associated with this problem?

**Answer:**

According to the cited reference: “Phytophotodermatitis is the most common phototoxic reaction seen in children. It is induced by sequential exposure to naturally occurring furocoumarin compounds (psoralens) and ultraviolet-A light; as a result, it is most common in the spring and summer. When psoralens are photoactivated, they covalently bind to pyrimidine bases on DNA strands, resulting in cell death.”

The most common plants associated with this problem are hogweed, parsnip, celery, carrots, fennel, dill, and citrus fruits (usually lemons and limes) (Moreau JF and English JC. Phytophotodermatitis. 2014 J Pediatr Adolesc Gynecol 27(2): 93-94)

**Wednesday, July 27, 2016**

**Question:**

According to the reference cited below, "Systemic allergic reactions to insect stings are reported by 0.3% to 7.5% of persons in the U.S. and Europe. Up to one fifth of these subjects will eventually experience severe life threatening reactions requiring emergency department admission." What are the risk factors for severe anaphylaxis (defined as anaphylactic shock, loss of consciousness, and/or cardiopulmonary arrest) to honeybee or vespid stings?

**Answer:**

According to the cited reference, "The frequency of this event (severe anaphylaxis) increased significantly with higher tryptase concentrations. Other factors significantly associated with severe reactions after a field sting were vespid venom allergy, older age, male sex, angiotensin-converting enzyme inhibitor medication, and one or more preceding field stings with a less severe systemic reaction." Serum tryptase concentrations are thought to represent a surrogate marker for mast cell numbers. One important preventive recommendation includes substitution of angiotensin-converting enzyme inhibitors in patients who have suffered severe anaphylaxis secondary to insect stings. (Rueff F et al. Predictors of severe systemic anaphylactic reactions in patients with Hymenoptera venom allergy: Importance of baseline serum tryptase. 2009 Allergy Clin Immunol 124:1047-1054)

**Tuesday, July 26, 2016**

**Question:**

What is the differential diagnosis of muscular spasms in heroin users?

**Answer:**

According to the cited reference: "The differential diagnosis of muscular spasms in heroin users includes tetanus, adulterant toxicity (such as strychnine, caffeine, amphetamines and phencyclidine), extra-pyramidal side effects from concomitant medication use or adulterants (e.g. dystonic reaction from an adulterant), opioid withdrawal, electrolyte abnormalities (e.g. hypocalcemia), and serotonin syndrome." (Manini A et al. A novel neuromuscular syndrome associated with clenbuterol-tainted heroin. 2008 Clin Tox 46:1088-1092)

**Monday, July 25, 2016**

**Question:**

What characterizes the syndrome of cannabinoid hyperemesis?

**Answer:**

According to the cited reference: "Presentation of cannabinoid hyperemesis syndrome occurs with cycles of symptom free intervals. This syndrome has been broken down to 3 phases: pre-emetic or prodromal, hyperemetic, and recovery. The prodromal phase can last for months to even years, with patients enduring morning sickness, anxiety, and abdominal pain. In this stage, patients usually can maintain normal eating habits and will continue their marijuana usage because they believe it is helping alleviate their nausea. The hyperemetic phase can last as few as 48 hours if treated with appropriate therapy. It is characterized by paroxysms of intense and persistent cyclic vomiting, upward of 5 times an hour, sometimes without warning. Patients also can have weight loss, abdominal pain, and dehydration. It is within this phase that patients typically begin to take compulsory hot water showers or baths. Patients find this to be the only alleviating measure to control symptoms and this readily becomes a learned behavior. The recovery phase can extend from days to months and is associated with general patient wellness, weight gain, regular frequency of bathing, and return of normal eating patterns." (Beech RA et al. Cannabinoid hyperemesis syndrome: A case report and literature review. 2015 J Oral Maxillofac Surg 73:1907-1910)

**Friday, July 22, 2016**

**Question:**

Urushiol is the potentially toxic oil found in the stems, roots, leaves and fruits of plants of the Toxicodendron species known as poison ivy, poison oak and poison sumac. What are the characteristics of urushiol and what sort of contact is usually required to release the oil onto the skin of an exposed individual?

**Answer:**

According to the cited reference: "Urushiol is colorless or slightly yellow in its natural state, but oxidize, polymerizes and turns black when exposed to air. It is non-volatile, dries quickly on fomites where it retains its antigenic potential in the dry state indefinitely (longevity is increased in dry climates and decreased in warm, moist climates). Usually, damage is required for plants to release the oil, therefore, slight contact with uninjured leaves is innocuous. More vigorous activities such as weeding or clearing brush, or cross country travel and bushwhacking, can transfer the oil onto the skin. As little as 2 mg can cause a reaction in sensitive individuals." (Gladman AC. Toxicodendron dermatitis: Poison ivy, oak and sumac. 2006 Wilderness Env Med 17(2): 120-128)

**Thursday, July 21, 2016**

**Question:**

The presence of which "diol" compound may result in false positive ethylene glycol levels identified by gas chromatographic methods?

**Answer:**

The presence of the chemical 2,3 butanediol may result in false positive ethylene glycol levels identified by gas chromatographic methods. (Jones AW et al. 2,3 butanediol in plasma from an alcoholic mistakenly identified as ethylene glycol by gas chromatographic analyses. 1991 Clin Chem 37(8): 1453-1455)

**Wednesday, July 20, 2016**

**Question:**

Nitrofurantoin is a commonly used medication for the treatment of uncomplicated lower urinary tract infections. Nitrofurantoin has been associated with pulmonary toxicity in some cases. What characterizes nitrofurantoin induced pulmonary toxicity?

**Answer:**

The cited reference reports: "Clinically, the acute reaction is characterized by fever, shortness of breath, cough and peripheral eosinophilia, usually within days to a few weeks of drug initiation. Chronic nitrofurantoin toxicity is typically associated with cough and slowly progressive dyspnea manifesting months to years after initiating therapy. Histologically, both forms manifest with a wide pattern of histological reactions including pulmonary fibrosis." (Kabbara WK and Kordahi MC. Nitrofurantoin-induced pulmonary toxicity: A case report and review of the literature. 2015 J Inf Pub Health 8:309-313)

**Tuesday, July 19, 2016**

**Question:**

Mesenteric venous thrombosis (MVT) is a known cause of intestinal ischemia and accounts for roughly 15% of all cases of mesenteric ischemia. In approximately 75% of cases of MVT, a prothrombotic state can be identified with coagulation disorders, neoplasia, intra-abdominal inflammatory states and portal hypertension among the most commonly reported causes. While MVT is most common in the 6<sup>th</sup> to 7<sup>th</sup> decade of life, young women have been reported to suffer from this disorder as well. Which pharmacological agents have been associated with the development of MVT in young women?

**Answer:**

In young females, the use of oral (as well as transdermal patch and vaginal ring) contraceptives reportedly accounts for up to 18% of cases of MVT. (Eilbert W et al. Acute mesenteric venous thrombosis with a vaginal ring contraceptive. 2014 Western J Med 15(4): 395-397)

**Monday, July 18, 2016**

**Question:**

Long-term occupational exposure to certain hardwood dusts has been associated with the development of cancer, in some workers, in which anatomic location?

**Answer:**

Long-term occupational exposure to certain hardwood dusts, (including oak, beech, birch, mahogany, teak and walnut) has been associated with the development of sino-nasal cancer. (Gori G et al. 2-methylanthraquinone as a marker of occupational exposure to teak wood dust in boatyards. 2009 Ann Occup Hyg 53(1): 27-32)

**Friday, July 15, 2016**

**Question:**

The Gaboon viper (*Bitis gabonica*) is the largest in size of all vipers and, on striking, is well known for the delivery of a large quantity of venom. One known effect of this venom is the development of coagulopathy. What characterizes the coagulopathy associated with the bite of the Gaboon viper?

**Answer:**

According to the cited reference: "Coagulation changes follow a typical pattern. Fibrinogen levels fall, probably as a result of activation of fibrinogen-fibrin conversion by the thrombin-like enzyme in the venom. As a result of this process, FDPs rise and prothrombin time becomes prolonged. Platelet count is almost invariably unaltered. .... [some cases have] demonstrated that patients may have a normal coagulation profile for some days after antivenom treatment, but can then deteriorate suddenly and without warning." (Marsh N et al. Gaboon viper (*Bitis gabonica*) envenomation resulting from captive specimens- A review of five cases. 2007 Clin Tox 45:60-64)

**Thursday, July 14, 2016**

**Question:**

The reference cited below notes that "The presence of water disinfection byproducts (DBPs) in swimming pools constitutes a public health concern." Chlorination is the most common disinfection method used in public and private pools. What are the DBPs of most concern that are formed when chlorine reacts with organic matter present in swimming pool water?

**Answer:**

The DBPs of most concern that are formed when chlorine reacts with organic matter present in swimming pool water are trihalomethanes, chloroform, bromoform, bromodichloromethane, and dibromochloromethane. The authors of the cited reference state: "in water samples chloroform is usually the most prevalent compound formed, although in the presence of bromine, brominated trihalomethanes may become more concentrated than chloroform." (Silva ZI et al. Trihalomethanes in Lisbon indoor swimming pools: Occurrence determining factors, and health risk classification. 2012 J Tox Env Health 75:878-892)

**Wednesday, July 13, 2016**

**Question:**

On January 9, 2014, an estimated 10,000 gallons of an industrial chemical, 4-Methylcyclohexanemethanol (MCHM), spilled into the Elk River just upstream from the Kanawha County municipal water intake in Charleston, West Virginia. This municipal water system serves nearly 300,000 people whose water was affected by the chemical spill. What is MCHM and what is it used for?

**Answer:**

4-methylcyclohexanemethanol (MCHM) is an alicyclic chemical used to process coal. MCHM does not explode or catch fire. As a class of organic alcohols, it has an obvious odor and is reported to smell like licorice. ( <http://emergency.cdc.gov/chemical/MCHM/westvirginia2014/mchm.asp>; accessed July 2016)

**Tuesday, July 12, 2016**

**Question:**

Chloroform, trichloromethane, was originally used as a general anesthetic agent. At present this compound is used primarily as a feedstock chemical in industry. Most human exposures to chloroform occur via inhalation with a few cases reported of intentional and/or accidental ingestion sometimes resulting in multi-organ injury. What is the metabolism of chloroform and specifically how does metabolism of this compound result in hepatic injury?

**Answer:**

According to the cited reference "Chloroform is metabolized by oxidative dehydrochlorination of its carbon-hydrogen bond to form phosgene, carbonyl sulfide, and hydrogen cyanide. The primary sites of metabolism are the liver and the kidneys. The reactive metabolites are prevented from covalently binding to microsomal proteins by hepatic glutathione (GSH). Phosgene depletes hepatocellular GSH and thus results in liver injury in the form of hepatocellular steatosis and necrosis." (Sridhar N et al. Chloroform poisoning- A case report. 2011 Renal Failure 33(10); 1037-1039)

**Monday, July 11, 2016**

**Question:**

What is phenibut?

**Answer:**

The cited reference notes that phenibut (beta-phenyl-gamma-butyric acid) is a GABA agonist "with greater activity at GABA<sub>B</sub> receptors compared with GABA<sub>A</sub>". The authors further point out that "it is structurally similar to baclofen which likewise has GABA<sub>B</sub> agonistic properties." Phenibut is marketed as a supplement on the internet. It is used as a therapeutic agent for anxiety and drug withdrawal states in Russia. (Downes MA et al. Acute behavioural disturbance associated with phenibut purchased via an internet supplier. 2015 Clin Tox 53:636-638)

**Friday, July 8, 2016**

**Question:**

What is "snake wine"?

**Answer:**

According to the cited reference, "snake wine" is a beverage that "contains more than 45% ethanol and whole venomous snakes". These authors further note: "Snake wine is generally preserved in an airtight, sealed container before it is drunk. Snake wine is consumed in certain Asian countries, including South Korea, for its presumed effect of invigorating ones energy level." The cited reference reports on severe coagulopathy after the ingestion of "snake wine". (Moon JM and Chun BJ. Severe coagulopathy after the ingestion of "snake wine" 2016 J Emerg Med 50(6): 848-851)

**Thursday, July 7, 2016**

**Question:**

Domoic acid is a toxin produced by a variety of marine alga and has been identified as the toxin that causes amnesic shellfish poisoning. Domoic acid has been detected in the viscera of a variety of marine invertebrates and vertebrates around the world. Which crab species has been identified as sometimes containing domoic acid?

**Answer:**

The cited reference notes: "high levels of domoic acid have been documented in [among other marine species].....Dungeness crabs (*Metacarcinus magister*). (Schultz IR et al. Domoic acid toxicokinetics in Dungeness crabs: New insights into mechanism that regulate bioaccumulation. 2013 Aquatic Toxicology 140-141:77-88)

**Wednesday, July 6, 2016**

**Question:**

What is so-called “crumb rubber”, what are the major uses for this material and what are the health concerns that have been raised with regard to this material?

**Answer:**

According to the US EPA, the term “crumb rubber”: “Refers to ground rubber pieces the size of sand or silt used in rubber or plastic products, or processed further into reclaimed rubber or asphalt products.” Approximately 30% of crumb rubber goes to the production of other rubber products, 31 % goes to playground mulch, 17% goes to the production of sports surfaces, 7% to the asphalt production industry and 6% goes to use in the automotive industry. One concern voiced by some is that exposure to crumb rubber may increase the risk of developing a variety of cancers. This notion has never been proven but research related to this question is ongoing.  
( [https://efmpub.epa.gov/sor\\_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do?details=&glossaryName=Recycling%20-%20State%20and%20Local](https://efmpub.epa.gov/sor_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do?details=&glossaryName=Recycling%20-%20State%20and%20Local); accessed June 2016 and (<https://www.epa.gov/chemical-research/tire-crumb-questions-and-answers>; accessed June 2016).

**Tuesday, July 5, 2016**

**Question:**

Which drug of abuse may be reported as falsely positive by urine immunoassay in individuals taking lamotrigine, MDPV, tramadol or venlafaxine?

**Answer:**

Phencyclidine (PCP) may be falsely positive, by urine immunoassay, in individuals taking lamotrigine, MDPV, tramadol or venlafaxine. (Saitman A et al. False positive interferences of common urine drug screen immunoassays: A review. 2014 J Anal Tox 38:387-396)

**Monday, July 4, 2016**

**Question:**

A variety of immunosuppressive and cytotoxic drugs including oxaliplatin, bevacizumab, sunitinib, sirolimus, gemcitabine, cyclosporine, as well as glucocorticoids and various vasopressive agents have been implicated in the development of which clinical entity characterized by headache, vomiting, altered mental status, blurred vision and seizures?

**Answer:**

The cited reference points out that the posterior reversible encephalopathy syndrome (PRES) is “most commonly associated with hypertensive encephalopathy, preeclampsia-eclampsia and hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome and immunosuppressive/cytotoxic drugs.” (Pedraza R et al. Posterior reversible encephalopathy syndrome: A review. 2009 Crit Care & Shock 12:135-143)

**Friday, July 1, 2016**

**Question:**

What are the clinical hallmarks of acyclovir-induced neurotoxicity and how is the diagnosis confirmed?

**Answer:**

According to the cited reference the “Presenting symptoms are neuropsychiatric and include disturbances in consciousness, myoclonus, seizures, coma, and death delusions. Most commonly, patients have had a preceding herpes zoster infection that has been treated with dosages of oral acyclovir or valacyclovir that were not properly calculated based on their level of renal dysfunction. Symptoms typically occur after the third or fourth dose and are rapidly progressive, especially if drug administration continues.” These authors further point out that “Once acyclovir-induced neurotoxicity is suspected, the diagnosis can be confirmed by identifying elevated cerebrospinal fluid levels of the acyclovir metabolite 9-carboxymethoxymethylguanine (9-CMMG). (Gentry JL and Peterson C. Death delusions and myoclonus: Acyclovir toxicity. 2015 Am J Med 128(7): 692-694)

**Thursday, June 30, 2016**

**Question:**

The nonnucleoside reverse-transcriptase inhibitor, Efavirenz, has been used as part of highly active antiretroviral therapy (HAART). Efavirenz use has resulted in false positive urine drug screens for which analyte?

**Answer:**

Efavirenz use has resulted in false positive urine drug screens for benzodiazepines. The authors of the cited reference report that “The major metabolite [of efavirenz] 8-hydroxy-efavirenz is responsible for this cross reactivity.” (Blank A et al. Efavirenz treatment and false-positive results in benzodiazepine screening tests. 2009 Clin Inf Dis 48:1787-1789)

**Wednesday, June 29, 2016**

**Question:**

What is Guarana?

**Answer:**

The cited reference reports: “Guarana, also called guaraná-da-amazônia, guaranaina, guaranauva, uarana or narana, is a species native to the Amazon region known for its stimulant and medicinal properties and used for centuries by indigenous communities of the Amazon.” The authors further note that “It is valued mainly for its stimulant property because of its high content of caffeine, which can be up to 6% in the seeds.” This article goes on to point out “In addition to caffeine, other purinic alkaloids were found in smaller proportions (below 0.3%) in guarana plants, including theobromine (3,7-dimethylxanthine) and theophylline (1,3-dimethyl-xanthine) (Schimpl FC et al. Guarana: Revisiting a highly caffeinated plant from the Amazon. 2013 J Ethnopharm 150:14-31)

**Tuesday, June 28, 2016**

**Question:**

What does the acronym “GRAS” signify?

**Answer:**

“GRAS” is an acronym for the phrase **G**enerally **R**ecognized **A**s **S**afe. Under sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act (the Act), any substance that is intentionally added to food is a food additive, that is subject to premarket review and approval by FDA, unless the substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use, or unless the use of the substance is otherwise excluded from the definition of a food additive.  
( <http://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/>; accessed June 2016)

**Monday, June 27, 2016**

**Question:**

What is The Toxic Substances Control Act of 1976 (known as TSCA)?

**Answer:**

The Toxic Substances Control Act of 1976 (known as TSCA) provides EPA with authority to require reporting, record-keeping and testing requirements, and restrictions relating to chemical substances and/or mixtures. Certain substances are generally excluded from TSCA, including, among others, food, drugs, cosmetics and pesticides. TSCA addresses the production, importation, use, and disposal of specific chemicals including [polychlorinated biphenyls \(PCBs\)](#), [asbestos](#), radon and [lead-based paint](#). This act was amended recently to include mandatory requirement for EPA to evaluate existing chemicals with clear and enforceable deadlines; new risk-based safety standard; increased public transparency for chemical information; and consistent source of funding for EPA to carry out the responsibilities under the new law.

(<https://www.epa.gov/laws-regulations/summary-toxic-substances-control-act>; accessed May 2016)

**Friday, June 24, 2016**



**Question:**

A substantial number of renal transplant patients annually are thought to succumb to cardiac arrhythmias and sudden cardiac death. What is the long-term impact of common immunosuppressive drugs (tacrolimus, cyclosporine A, everolimus, and azathioprine) on QTc and PR intervals in renal transplant patients?

**Answer:**

One recent study reported on 98 kidney transplant recipients whose post transplant QTc intervals were prolonged significantly in comparison to pre-transplant QTc. The authors of this study concluded "QT prolongation, a marker of risk for arrhythmias and sudden death, is highly prevalent among kidney transplant patients receiving different classes of immunosuppressive drugs." The authors of this work go on to warn "other drugs with QT prolongation potential should also be used cautiously in patients receiving immunosuppressive agents." (Ikitimur B et al. Long term impact of different immunosuppressive drugs on QT and PR intervals in renal transplant patients. 2015 Ann Noninvasive Electrocardiol 20(5): 426-432)

**Thursday, June 23, 2016**

**Question:**

Which chemical, used in the manufacture of white paint pigment, may result in skin burns as well as permanent ocular damage if unprotected exposure occurs?

**Answer:**

Titanium tetrachloride. According to ATSDR this chemical "can be very irritating to the skin, eyes, mucous membranes, and the lungs. Titanium tetrachloride is corrosive because it reacts strongly with water to produce hydrochloric acid. The reaction products, especially hydrochloric acid, cause the harmful health effects and burns that can occur after exposure to titanium tetrachloride. Breathing in large amounts of titanium tetrachloride can injure the lungs seriously enough to cause death. We do not know how much of the compound is necessary to cause death. After short-term exposure to titanium tetrachloride, less serious respiratory system effects can include coughing and tightness in the chest. More severe effects can include chemical bronchitis or pneumonia, and congestion of the mucous membranes of the upper respiratory tract. These effects can cause long-term effects such as the narrowing of the vocal cords, windpipe, and upper airways. Although there are no data on swallowing titanium tetrachloride, it is likely that eating large amounts of this chemical could also cause death." (Toxicological Profile for Titanium Tetrachloride. 1997 ATSDR. <http://www.atsdr.cdc.gov/toxprofiles/tp101.pdf>; accessed May 2016)

**Wednesday, June 22, 2016**

**Question:**

The crown-of-thorns starfish (*Acanthaster planci*) is a marine creature with venom-containing spines. What is the toxin contained in these spines and what clinical effects have been reported following human contact with this venom delivered by the crown-of-thorns? What is the geographic range of this marine creature?

**Answer:**

*Acanthaster planci* delivers a toxin containing plancitoxin I and II. According to the cited reference contact with *A. planci* spines can result in "extremely painful wounds, redness, and swelling but also serious systemic reactions such as hemolysis, paralysis and liver damage." Anaphylaxis and anaphylactic shock have also been reported. The crown-of-thorns starfish is reported to inhabit tropical and sub tropical coral reefs from the Red Sea to the Indo-Pacific Ocean. However the authors of the cited reference note: "Due to recent changes in the marine environment, most notably global warming, the habitat of the crown-of-thorns starfish has extended even farther..." (Ihama Y et al. Anaphylactic shock caused by sting of crown of thorns starfish (*Acanthaster planci*). 2014 For Sci Int 236:e5-e8)

**Tuesday, June 21, 2016**

**Question:**

Who was Gregorius Agricola and what role did he play in the evolution of occupational toxicology?

**Answer:**

Gregorius Agricola was a 15<sup>th</sup> Century scholar and scientist sometimes known as "the father of mineralogy". His most famous work was *De Re Metallica* in which he reported on work hazards for miners including occupational lung disease in miners and lung cancer in uranium miners. (Langard S. Gregorius Agricola memorial lecture: lung cancer-A work related disease for 500 years as predicted by Agricola. 2015 J Trace Elements Med Biol 31:214-218)

**Monday, June 20, 2016**

**Question:**

Black pigmentation of the tongue has been reported to be associated with which drug used to treat dyspepsia? What is the mechanism for the production of this black pigmentation and how does this drug-related hyperpigmentation differ from so-called "black hairy tongue"?

**Answer:**

Bismuth subsalicylate use has been reported to cause black pigmentation of the tongue. According to the cited reference "Anaerobic bacteria in the mouth are able to produce hydrogen sulfide. Bismuth subsalicylate can react with the hydrogen sulfide to produce bismuth sulfide. Bismuth sulfide is a highly insoluble black salt that is responsible for producing the darkening of the tongue in these individuals." This drug related lingual hyperpigmentation differs from "black hairy tongue" in that acquired (due to drugs) black tongue does not involve enlargement of the filiform papillae of the tongue that is typical of black hairy tongue. (Cohen PR. Black tongue secondary to bismuth subsalicylate: Case report and review of exogenous causes of macular lingual pigmentation. 2009 J Drugs Derm 8(12): 1132-1137)

**Friday, June 17, 2016**

**Question:**

Rifabutin, a semisynthetic derivative of rifamycin, is used in the treatment of *Mycobacterium avium* complex disease. What ocular complication of this therapy occurs primarily in patients suffering from HIV infection?

**Answer:**

Uveitis has been reported in patients suffering from HIV infection who are treated with rifabutin. (Olesen HH and Krag S. Rifabutin associated uveitis in a child. 2005 Ped Inf Dis J. 24(11): 1023-1025)

**Thursday, June 16, 2016**

**Question:**

What is ioderma? What is the pathophysiology of this problem and what is the recommended treatment?

**Answer:**

According to the cited reference "Iododerma is a skin eruption in response to iodine exposure. This patient [depicted in the associated image published with the cited reference] developed generalized pustular eruptions with multiple coalescing vesicles and pus-filled bullae hours after receiving iodinated contrast material for an imaging study. The pathogenesis is not clearly understood, with delayed iodine clearance and the induction of neutrophil degranulation described as possible mechanisms. Skin eruptions [in the published case] resolved 4 weeks later after treatment with thalidomide." (Image Challenge. NEJM <http://www.nejm.org> June 15, 2016 DOI: 10.1056/NEJMoa1604037)

**Wednesday, June 15, 2016**

**Question:**

What are erabutoxins?

**Answer:**

Erabutoxins are neurotoxins isolated from the venom of certain sea snakes including the sea snake *Laticauda semifasciata*. The cited reference notes "The short neurotoxins to which erabutoxins belong act by blocking the nicotinic acetylcholine receptor on the post synaptic membrane in a manner similar to that of curare." (Tamiya N and Yagi T. Studies on sea snake venom. 2011 Proc Jpn Acad Ser B 87(3): 41-52)

**Tuesday, June 14, 2016**

**Question:**

Over the past decade, the use of energy drinks has been implicated in a variety of cardiovascular catastrophes. One theory is that detrimental effects to platelet and endothelial function may play a role. While the constituents may vary between commercially available energy drinks, how does energy drink consumption effect platelet and endothelial function?

**Answer:**

One recent study examined both platelet function and endothelial function one hour after the consumption of 250 mL of a sugar free energy drink. These investigators reported: "Compared with baseline values, there was a significant increase in platelet aggregation following energy drink consumption while no change was observed with control." These authors concluded, "Energy drink consumption acutely increases platelet aggregation and decreases endothelial function in healthy young adults." The authors noted however, "This study did not attempt to determine which components of energy drinks might be responsible for [their] findings". (Worthley MI et al. Detrimental effects of energy drink consumption on platelet and endothelial function. 2010 Am J Med 123:184-187)

**Monday, June 13, 2016**

**Question:**

What is the rationale for the belief that commercially available caffeine containing energy drinks may contain far more caffeine than is indicated on the product label?

**Answer:**

The cited reference notes: "Common additives [to energy drinks], however, such as guarana, kola nut, yerba mate and cocoa, also have stimulant, cardiac and hematologic activity. These ingredients are often non-standardized in their caffeine content, sometimes considered as masked caffeine. Hence the actual amount of caffeine content in energy drinks may be higher than that reported in their labels." (Seifert SM et al. Health effects of energy drinks on children, adolescents, and young adults. 2011 Pediatrics 127:511-528 as cited in Seifert SM et al. An analysis of energy drink toxicity in the National Poison Data System. 2013 Clin Tox 51:566-574)

**Friday, June 10, 2016**

**Question:**

Which organism is known as the most venomous marine animal in the world? How are the toxins produced by this animal characterized? What are the systemic reactions reported to be associated with exposure to this animal?

**Answer:**

The box jellyfish (*Chironex fleckeri*) is known as the most venomous marine animal in the world. The cited reference notes "The majority of toxins are composed of a complex mixture of polypeptides and proteins, including hemolytic, cardio- toxic, and dermatonecrotic toxins." These authors also point out: "Systemic reactions include muscle spasm, pallor, headache, malaise, fever, nausea, vomiting, respiratory distress, hemolysis, and acute renal failure. In fatal cases, cardiovascular and respiratory arrest develop rapidly." (Thaikruea L et al. Review of fatal and severe cases of box jellyfish envenomation in Thailand. 2015 Asia-Pacific J Pub Health 27(2):NP 1639-NP1651)

**Thursday, June 9, 2016**

**Question:**

What is the probable cause for the green colored urine that can sometimes be seen in patients who have received the drug propofol?

**Answer:**

According to the cited reference: "Propofol is metabolized in the liver and excreted in the urine predominantly as the 1-glucuronide, 4-glucuronide and 4-sulfate conjugates of 2,6-diisopropyl-1,4 quinol. Green discoloration of urine is attributed to the presence of these phenolic metabolites." These authors also note "In addition to urine, reports of green discoloration of the hair and liver after propofol administration implicate these phenols." (Blakey SA and Hixson-Wallace JA. Clinical significance of rare and benign side effects: propofol and green urine. 2000 Pharmacotherapy 20(9): 1120-1122)

**Wednesday, June 8, 2016**

**Question:**

Loperamide is an antidiarrheal agent available over the counter. The use of this drug has been reported to be on the increase per national poison center data. What is the basis for this apparent increase in use?

**Answer:**

According to the cited reference: "Loperamide is an over the counter antidiarrheal with mu-opioid agonist activity. ....Recently, oral loperamide abuse as an opioid substitute has been increasing among patients attempting to self-treat their opioid addiction". (Eggleston W, Clark KH and Marraffa JM. Loperamide abuse associated with cardiac dysrhythmia and death. 2016 Ann Emerg Med IN PRESS [http://www.annemergmed.com/article/S0196-0644\(16\)30052-X/pdf](http://www.annemergmed.com/article/S0196-0644(16)30052-X/pdf))

**Tuesday, June 7, 2016**

**Question:**

"Medication sharing" involves the lending or borrowing of prescription medications with the ultimate use of those medicines by individuals who were not intended to receive those medicines. What is the prevalence rate for this potentially dangerous practice?

**Answer:**

According to the cited systematic review of this topic, "The prevalence rate for borrowing someone's prescription medication was 5% to 51.9% and for lending prescription medication to someone else was 6% to 22.9%. A wide range of medicines were shared between family members, friends and acquaintances." (Beyene KA et al. Medication sharing: A systematic review of the literature. 2014 Am J Public Health 104(4):e15-e26)

**Monday, June 6, 2016**

**Question:**

What is the phenomenon sometimes known as a "plumbogram"?

**Answer:**

The so-called "plumbogram" is a radiologic manifestation of lead arthropathy. The "plumbogram" occurs when a lead containing bullet or bullet fragment(s) lodge in a joint space and over time break down resulting from contact with acidic synovial fluid in combination with joint motion. Lead-containing fluid may then create a radio-dense outline of the joint cavity resulting in what is sometimes called a "lead arthrogram" or "plumbogram". (Fernandes JL et al. Lead arthropathy: radiologic, CT and MRI findings. 2007 Skeletal Radiol 36:647-657)

**Friday, June 3, 2016**

**Question:**

What are the post transplantation issues for patients treated with amiodarone on a long-term basis and who subsequently undergo heart transplantation?

**Answer:**

Precedent therapy with amiodarone may pose special risks for patients who undergo heart transplantation. According to the cited reference, “Amiodarone is a known inhibitor of transplant drug metabolism and can therefore potentiate the toxicity of these dangerous medications. Additionally, due to its long half-life and extensive volume of distribution, redistribution of amiodarone from recipient body tissue to the transplanted heart has been observed. One case series of seven heart transplant recipients treated with oral amiodarone for at least 3 weeks prior to transplantation observed an accumulation of amiodarone in the transplanted heart as early as 1 week post-transplantation. The concentration of amiodarone peaked at 2 weeks posttransplant and remained detectable up to 12 weeks posttransplant. The redistribution into donor myocardial tissue can result in prolonged amiodarone exposure, which could exacerbate post-transplant arrhythmias and adversely affect graft survival. (Giardina EGV et al. Myocardial amiodarone and desethylamiodarone concentrations in patients undergoing cardiac transplantation. 1990 J Am Coll Cardiol 16(4): 943–947 and Nanas JN et al. Redistribution of amiodarone in heart transplant recipients treated with the drug before operation. 1997 J Heart Lung Transplant 4:387–389, as cited in Jennings DL et al. Impact of pre-implant amiodarone exposure on outcomes in cardiac transplant recipients. 2015 Heart Fail Rev 20:573–578)

**Thursday, June 2, 2016****Question:**

Which medications are associated with false positive phencyclidine urine screens?

**Answer:**

The authors of the cited reference concluded: “False-positive urine screens for PCP are associated with tramadol and dextromethorphan and may also occur with diphenhydramine. Positive PCP screens associated with alprazolam, clonazepam, and carvedilol were also associated with polysubstance abuse.” (Rengarajan A and Mullins ME. How often do false-positive phencyclidine urine screens occur with use of common medications? 2013 Clin Tox 51:493-496)

**Wednesday, June 1, 2016****Question:**

What is the FDA’s so called “boxed warning”?

**Answer:**

The cited reference notes that “boxed warnings” are sometimes known as “black box warnings” and were initiated by the FDA in 1979. These authors note: “boxed warnings are the most serious level of warning provide by the Food and Drug Administration (FDA).” The authors further point out: “The FDA typically reserves such warnings for medications in which a severe adverse drug reaction may lead to death or serious injury.” They go on to state: “They are aimed at the prescribing health care practitioner and are prominently displayed in the packaging insert surrounded by a black box. The contents of the warnings typically highlight vulnerable patient populations, drug-drug interactions and dosing risks, or information on early detection of reversible conditions. The approval of a new drug by the FDA may be contingent upon the placement of a boxed warning.” (Smollin CG et al. Recognition and knowledge of medications with black box warnings among pediatricians and emergency physicians. 2016 J Med Tox 12:180-184)

**Tuesday, May 31, 2016****Question:**

An occupational and environmental chemical disaster in the United States involved manufacturer, “Life Science Products Company”, operating in Hopewell, Virginia, (1974-1975), caused millions of dollars of damage and demonstrated the links between hazards inside the factory and those outside the factory. Which infamous chemical pesticide was at issue in this disaster?

**Answer:**

The pesticide at issue in the Hopewell disaster was Kepone, the registered trade name of Allied Chemical Corp. for the compound known as chlordane. Kepone is a polychlorinated hydrocarbon and is known for its prolonged environmental persistence. (Reich MR and Spong JK. Kepone: A chemical disaster I Hopewell, Virginia. 1983 Int J Health Services 13(2): 227-246 and The National Toxicology Program- <http://ntp.niehs.nih.gov/ntp/roc/content/profiles/kepone.pdf>; accessed May 2016)

**Monday, May 30, 2016****Question:**

Which toxins are contained in the plant purple foxglove (*Digitalis purpurea*) as compared with the plant Grecian foxglove (*Digitalis lanata*)? Which plant has reportedly been associated with more deaths due to ingestion?

**Answer:**

*Digitalis purpurea* contains digitoxin and gitoxin in the leaves and digitalin in the seeds while *Digitalis lanata* contains digoxin and lanatosides A-E and associated glycosides. According to the cited article, “Although death because of the toxic effects of the therapeutic *D. lanata* extract, digoxin has been reported, there are no reported cases of fatal *D. purpurea* (digitoxin) plant intoxication in humans in the literature. It is striking that only a leaf or two are potentially fatal.” (Ramlakhan SL and Fletcher AK. It could have happened to Van Gogh: A case of fatal purple foxglove poisoning and review of the literature. 2007 Eur J Emerg Med 14:356-359)

**Friday, May 27, 2016****Question:**

What is SBIRT?

**Answer:**

“SBIRT” stands for “Screening”, “Brief Intervention”, and “Referral to Treatment”. SBIRT is a comprehensive, integrated, public health approach to the delivery of early intervention and treatment services for persons with substance use disorders, as well as those who are at risk of developing these disorders. Primary care centers, hospital emergency departments, trauma centers, and other community settings provide opportunities for early intervention with at-risk substance users before more severe consequences occur.

Screening quickly assesses the severity of substance use and identifies the appropriate level of treatment.

Brief intervention focuses on increasing insight and awareness regarding substance use and motivation toward behavioral change.

Referral to treatment provides those identified as needing more extensive treatment with access to specialty care. (<http://www.samhsa.gov/sbirt/about>; accessed May 2016)

**Thursday, May 26, 2016****Question:**

Promethazine is a phenothiazine derivative sometimes prescribed for the treatment of nausea, vomiting and motion sickness. Recent reports note that the use of this drug is common among chronic opiate users and has been identified as an adulterant in various fentanyl-containing products available from illicit street sale. What is the likely purpose for the use of promethazine among chronic opiate users and as an adulterant in fentanyl sold on the street for illicit use?

**Answer:**

Promethazine is thought to potentiate the “high” from opioids. (Lynch KL, et al. Promethazine use among chronic pain patients. 2015 Drug Alcohol Depend, 150:92–97 as cited in Counterfeit Norco Poisoning Outbreak — San Francisco Bay Area, California, March 25–April 5, 2016 Morbidity and Mortality Weekly Report, April 29, 2016 / 65(16); 420–423)

**Wednesday, May 25, 2016****Question:**

Workers in which industries might be exposed to gallium compounds and thus potentially at risk for gallium related toxicity?

**Answer:**

According to the cited reference: "Gallium compounds are used notably in the manufacture of optoelectronic devices. Gallium is also used in some dental materials and for treatment of cancer." These authors go on to state "Workers who produce semiconductors or who handle gallium compounds in scientific or laboratory settings are at risk. Gallium poisoning has not yet presented a concern for patients with restorations containing gallium alloys. However, dentists need to be aware that gallium poisoning is possible." (Ivanoff CS et al. Gallium poisoning: A rare case report. 2012 Food Chem Tox 50: 212-215)

**Tuesday, May 24, 2016****Question:**

What potentially life threatening hematologic manifestation has been reported in cases of *Loxosceles reclusa* bites?

**Answer:**

The cited reference notes: "L. reclusa envenomation can result in a life-threatening hemolytic anemia with mortality despite supportive measures". These authors go on to describe "Our studies indicate that this hemolytic process is complement mediated and is substantially reduced by eculizumab in vitro. Because venom from L. reclusa results in a reduction of detectable glycophorin A, glycophorin A levels should be further investigated as a supportive test for management of Loxosceles venom exposure. A clinical trial to establish the utility of glycophorin A expression and eculizumab therapy in the diagnosis and treatment of L. reclusa-mediated hemolysis is needed." (Gehrie EA, Nian H, Young PP (2013) Brown Recluse Spider Bite Mediated Hemolysis: Clinical Features, a Possible Role for Complement Inhibitor Therapy, and Reduced RBC Surface Glycophorin A as a Potential Biomarker of Venom Exposure. 2013 PLoS ONE 8(9): e76558. doi:10.1371/journal.pone.0076558)

**Monday, May 23, 2016****Question:**

Which substance, whose principal psychoactive effects are mediated by serotonin 2A, acts as a prodrug for the serotonin receptor agonist psilocin (4-hydroxy-dimethyltryptamine) has been considered as a possible adjunct for treatment resistant depression?

**Answer:**

Psilocybin, a naturally occurring plant alkaloid found in *Psilocybe* mushrooms acts as a prodrug for the serotonin receptor agonist psilocin (4-hydroxy-dimethyltryptamine) has been considered as a possible adjunct for treatment resistant depression. (Carhart-Harris RL et al. Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study. www.thelancet.com/psychiatry Published online May 17, 2016 [http://dx.doi.org/10.1016/S2215-0366\(16\)30065-7](http://dx.doi.org/10.1016/S2215-0366(16)30065-7))

**Friday, May 20, 2016****Question:**

Parenteral nutrition is a critical aspect of nutritional support for neonates. Contamination of parenteral nutrition compounds by which substance has been reported to cause renal, metabolic and neurologic sequelae in neonates?

**Answer:**

Aluminum as a contaminate of parenteral nutrition compounds has been reported to cause renal, metabolic and neurologic sequelae in neonates. The authors of the cited reference note: "Aluminum toxicity has been described in patients of all ages who are receiving a variety of therapies, including dialysis phosphate-binding medications and parenteral nutrition. Neonates are at an increased risk of aluminum toxicity because of anatomic, physiologic and nutrition related factors not present in other populations." (Wier HA and Kuhn RJ. Aluminum toxicity in neonatal parenteral nutrition: What can we do? 2012 Ann Pharmacother 46(1): 137-140)

**Thursday, May 19, 2016****Question:**

Blue cohosh (*Caulophyllum thalictroides* (L.) Michx.; *C. giganteum* (Farw.) Loconte & W.H. Blackw; Family Berber- idaceae) is a plant that has been used by Native Americans, midwives and herbal medicine practitioners. What potential therapeutic actions have traditionally been ascribed to the use of blue cohosh?

**Answer:**

The therapeutic actions that have traditionally been ascribed to the use of blue cohosh include use as: an abortifacient, emetic, anti-inflammatory, emmenagogue, anti-pyretic, diuretic, expectorant, hypoglycemic, spasmogenic, uteronic, and vaso-constrictor, among many others. (radder JI and Pawar RS. Primary constituents of blue cohosh: quantification in dietary supplements and potential for toxicity. 2013 Anal Bioanal Chem 405:4409-4417)

**Wednesday, May 18, 2016****Question:**

What is entomotoxicology?

**Answer:**

According to the cited reference: "Entomotoxicology studies the application of toxicological analysis to carrion-feeding insects in order to identify drugs and toxins present on intoxicated tissues. Entomotoxicology also investigates the effects caused by such substances on arthropod development in order to assist the forensic PMI estimates." (Goff ML and Lord WD. Entomotoxicology: a new area for forensic investigation 1994 Am. J. Forensic Med. Pathol., 15 :51-57 as cited in Introna F. Entomotoxicology. 2001 For Sci International 120 (1-2): 42-47)

**Tuesday, May 17, 2016****Question:**

Why is cyanide used in gold mining and what percentage of global cyanide usage is by the gold mining industry?

**Answer:**

Cyanide effectively and efficiently extracts gold from ore. While a number of other chemicals are available to extract gold, such as chloride bromide, thiourea, and thiosulfate, these form less stable complexes with gold and thus require more aggressive conditions and oxidants to dissolve the gold. The alternative chemicals are generally more expensive to use and also present risks to health and the environment that are similar to or greater than that presented by cyanide. The industry continues to search for cost-effective and environmentally friendly alternatives to cyanide.

Of the approximately 1.1 million tonnes of hydrogen cyanide produced annually worldwide, about 6% is used to produce cyanide reagents for gold processing. The remaining 94% is used in other industrial applications which include the production of nylon, plastics, adhesives, fire retardants, cosmetics, pharmaceuticals, food processing and as an anti-caking additive for table and road salts. ( <http://www.cyanidecode.org/about-cyanide-code-faq>; accessed May 2016)

**Monday, May 16, 2016****Question:**

What is the occupational disorder known as "tulip fingers"?

**Answer:**

"Tulip fingers", is a allergic contact dermatitis that may develop in workers in the horticultural industry and trade who handle tulip flowers and stalks. This manifests as digits that appear to be hyperkeratotic with multiple small painful fissures. This results from exposure to tuliposide A, a glycoside compound that hydrolyzes to form alpha-methylene butyrolactone. This hydrolysis product is the likely specific culprit allergen that causes "tulip fingers". (Bruze M. et al. Occupational dermatoses in nursery workers. 1996 Am J Contact Derm 7(2): 100-103)

**Friday, May 13, 2016**

**Question:**

The Manchineel tree (*Hippomane mancinella*) produces an extremely potent toxin. What are the reported adverse effects in humans that may come into contact with the sap of this tree which is found in Florida, the West Indies and Central and South America?

**Answer:**

According to the cited reference "Exposure to the toxic sap (which contains diterpene esters of the tiglane phorbol and daphnane types) can cause severe dermatitis and ophthalmitis consisting of erythema, blistering, swelling, inflammation, pustulation, and conjunctivitis with painful burning sensation typical of Chemical Irritant Contact Dermatitis (CICD). Exposure most commonly takes place when individuals take refuge from the rain under a Manchineel tree. Ingestion of the Manchineel fruit (Beach Apple or "Manzanilla de la muerte") can cause severe swelling, ulceration, and hemorrhage of the oral and gastrointestinal mucosa which has been reported to be fatal in extreme cases. Systemic manifestations can be significant and persistent bradycardia requiring permanent pacemaker insertion has been ascribed to Manchineel toxicity." (Blue LM et al. Manchineel dermatitis in North American students in the Caribbean. 2011 J Travel Med 18(6): 422-424)

**Thursday, May 12, 2016**

**Question:**

What are the primary industrial uses for the compound vanadium?

**Answer:**

Vanadium is mostly combined with other metals to make special metal mixtures called alloys. Vanadium in the form of vanadium oxide is a component in special kinds of steel that is used for automobile parts, springs, and ball bearings. Most of the vanadium used in the United States is used to make steel. Vanadium oxide is a yellow-orange powder, dark-gray flakes, or yellow crystals. Vanadium is also mixed with iron to make important parts for aircraft engines. Small amounts of vanadium are used in making rubber, plastics, ceramics, and other chemicals. ( <http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=50:accessed> may, 2016)

**Wednesday, May 11, 2016**

**Question:**

FDA recently issued a warning regarding the antipsychotic medication olanzapine. What adverse effect did they warn about?

**Answer:**

FDA is adding a new warning to the drug labels for all olanzapine-containing products that describes the Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).

A search of the FDA Adverse Event Reporting System (FAERS) database identified 23 cases of DRESS reported with olanzapine worldwide since 1996, when the first olanzapine-containing product was approved. FAERS includes only reports submitted to FDA, so there are likely to be additional cases about which FDA is unaware. One patient taking olanzapine experienced DRESS and died; however, this patient was taking multiple medicines that could also have contributed to death.

( <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm500123.htm>; accessed May 2016)

**Tuesday, May 10, 2016**

**Question:**

Hyperthyroidism is a common problem in pregnancy and is usually treated with the amide drugs methimazole (MMI) and propylthiouracil (PTU). In pregnancy, PTU is generally used to treat maternal hyperthyroidism during the first trimester and then therapy is switched to MMI for the duration of the pregnancy. What is the rationale for this pattern of drug usage in treating hyperthyroidism during pregnancy?

**Answer:**

According to the cited reference, the reason for the above-mentioned usage pattern for MMI and PTU in treating hyperthyroidism during pregnancy is the fact that "MMI causes a specific pattern of rare teratogenic effects after first trimester exposure.....". MMI use during the first trimester of pregnancy has been associated with aplasia cutis congenital, choanal atresia, and tracheoesophageal fistulas. (Hackmon R et al. The safety of methimazole and propylthiouracil in pregnancy: A systematic review. 2012 J Obstet Gyn Can 34(11): 1077-1086)

**Monday, May 9, 2016**

**Question:**

Epidemiologic studies show a consistent association between outbreaks of the disease known as konzo and chronic dietary reliance on foodstuffs derived from insufficiently processed toxic and cyanogenic cassava (also known as manioc or tapioca). What are the criteria for the clinical diagnosis of konzo?

**Answer:**

The cited reference notes: "The World Health Organization has adopted the following epidemiologic criteria for the disease: 1) an abrupt onset (<1 week) of weakness in legs and a non-progressive course of the disease in a formerly healthy person, 2) a symmetrical spastic abnormality when walking and/or running, and 3) bilaterally exaggerated knee and/or ankle jerks without signs of disease of the spine." (Tshala-Katumbay D et al. Cassava food toxins, konzo disease and neurodegeneration in sub-Saharan Africans. 2013 Neurology 80(10): 949-951)

**Friday, May 6, 2016**

**Question:**

What percent of chronic benzodiazepine users will experience protracted moderate to severe withdrawal symptoms (including emergent anxiety and depressive symptoms as well as potentially lethal seizures) upon cessation?

**Answer:**

According to the cited reference, 15-44% of chronic benzodiazepine users will experience protracted moderate to severe withdrawal symptoms (including emergent anxiety and depressive symptoms as well as potentially lethal seizures) upon cessation. (De las Cuevas et al. The severity of dependence scale as a screening test for benzodiazepine dependence: SDS validation study. 2000 Addiction 95:245-250 as cited in Lugoboni F and Quaglio G. Exploring the dark side of the moon: the treatment of benzodiazepine tolerance. 2013 Br J Clin Pharmacol 77(2): 239-241)

**Thursday, May 5, 2016**

**Question:**

What was the so-called "LEAP" trial and what did it show?

**Answer:**

"LEAP" stands for "Learning Early About Peanut Allergy trial". According to the cited references, ".....the compelling results of the Learning Early About Peanut Allergy trial.....showed that the early consumption of peanut by high-risk infants dramatically decreased their risk of the development of peanut allergy." (DuToit G et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. 2015 NEJM 372:803-813 as cited in Wong GWK. Preventing food allergy in infancy-Early consumption. 2016 NEJM 374(18): 1783-1784)

**Wednesday, May 4, 2016**

**Question:**

What is the efficacy of succimer in children with low level organic mercury exposure?

**Answer:**

One study of more than 700 children reported: "The adjusted mean organic mercury concentration in the succimer group relative to the placebo group fell from 99% at baseline to 82% after 3 courses of treatment (  $P$  for trend = .048), but this resulted from the prevention of the age-related increase in the succimer group." These authors felt that it was "unlikely" that succimer would be of clinical utility in young children with low level organic mercury exposure. (Cao Y et al. Efficacy of succimer chelation of mercury at background exposures in toddlers: A randomized trial. 2011 J Pediatr 158:480-485)

**Tuesday, May 3, 2016****Question:**

What is Stoddard Solvent?

**Answer:**

Stoddard solvent is a colorless, flammable liquid that smells and tastes like kerosene. It will turn into a vapor at temperatures of 150-200°C. Stoddard solvent is a petroleum mixture that is also known as dry cleaning safety solvent, petroleum solvent, and varnoline; its registered trade names are Texsolve S® and Varsol 1®. It is a chemical mixture that is similar to white spirits. Stoddard solvent is used as a paint thinner; in some types of photocopier toners, printing inks, and adhesives; as a dry cleaning solvent; and as a general cleaner and degreaser. (<http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=73>; accessed March 2016)

**Monday, May 2, 2016****Question:**

The use of fluoroquinolone antibiotics has been linked to a number of medical problems including seizures, tendonopathies, torsades de pointes, hepatotoxic effects, and dysglycemia. Which important vascular and ocular effects have been recently suggested to be associated with fluoroquinolone use?

**Answer:**

In addition to seizures, tendonopathies, torsades de pointes, hepatotoxic effects, and dysglycemia, recent literature has linked an increased risk for aortic dissection, aortic aneurysm and retinal detachment to fluoroquinolones use. (Lee CC et al. Risk of aortic dissection and aortic aneurysm in patients taking oral fluoroquinolones. 2015 JAMA Int Med 175(11): 1839-1847)

**Friday, April 29, 2016****Question:**

What is the molecular adduct formed by the reaction of formaldehyde with hemoglobin that has been proposed as a biomarker for formaldehyde exposure?

**Answer:**

According to the cited reference "N-Methylvaline is a molecular adduct that is formed by the reaction of formaldehyde with hemoglobin. Bono et al. (2006) demonstrated an association between formaldehyde exposure in plywood and laminate factory workers (n=21) and the occurrence of N-methylvaline in blood. However, this assay could not distinguish between subjects exposed to formaldehyde through tobacco smoke, on the one hand, and nonsmokers, on the other. (Bono R, Vincenti M, Schiliro T, et al. N-methylvaline in a group of subjects occupationally exposed to formaldehyde. 2006 Toxicol Lett 161(1):10-17 as cited in Addendum to the Toxicological Profile for Formaldehyde, ATSDR, 2010. [http://www.atsdr.cdc.gov/toxprofiles/formaldehyde\\_addendum.pdf](http://www.atsdr.cdc.gov/toxprofiles/formaldehyde_addendum.pdf); accessed April 2016)

**Thursday, April 28, 2016****Question:**

It has been reported that 70% of illicit cocaine may be adulterated with the drug levamisole. What are the specific clinical syndromes likely related to levamisole-adulterated cocaine?

**Answer:**

According to the cited reference, "Three distinct clinical syndromes seem to exist: CIMDL (cocaine-induced midline destructive lesions), levamisole-associated agranulocytosis and levamisole associated cutaneous vasculopathy." (Specks U. The growing complexity of the pathology associated with cocaine use. 2011 J Clin Rheumatol 17:167-168 as cited in Laroque A and Hoffman RS. Levamisole in cocaine: Unexpected news from an old acquaintance. 2012 Clin Tox 50(4): 231-241)

**Wednesday, April 27, 2016****Question:**

What are so-called "drug dreams"?

**Answer:**

Drug dreams are also known as "using dreams". These are dreams centered around the act of using specific drugs. The cited reference reports on a study that notes up to 74% of users of illicit drugs report having at least one drug dream over the course of a 36 week observational period. These authors also describe the successful use of the alpha-1 receptor antagonist, prazosin in treating drug dreams. (Gopalakrishna G et al. Two case reports on the use of prazosin for drug dreams. 2016 J Addict Med 10(2): 131-133 and Yee T et al Drug dreams in outpatients with bipolar disorder and cocaine dependence. 2004 J Nerv Ment Dis 192(3): 238-242)

**Tuesday, April 26, 2016****Question:**

The chemical paraphenylenediamine (PPD) is a component of many hair dyes although it has been banned in many countries. In some cultures, PPD is combined with henna to dye the palms and/or soles. Poisoning involving the ingestion of paraphenylenediamine is commonly a part of suicidal gestures in Morocco, India and various countries in the Middle East. What clinical findings are associated with PPD ingestion?

**Answer:**

The cited reference notes "Ingestion of PPD causes rapid development of edema of the face, neck, pharynx, tongue and larynx initially and rhabdomyolysis later. Finally, an acute renal failure supervenes as renal tubular necrosis occurs due to the deposits of the toxic metabolites of PPD." (Prabhakaran A. Paraphenylene diamine poisoning. 2012 Indian J Pharmacol 44(3): 423-424)

**Monday, April 25, 2016****Question:**

So-called artisanal small-scale gold mining (ASGM) provides a livelihood for tens of millions of people around the world, especially in developing countries. ASGM is defined as the extraction of gold using simple techniques. ASGM results in exposure and potential toxicity to which toxicant?

**Answer:**

The cited reference notes: "An estimated 640-1,350 tons of mercury (Hg) is released per annum into the environment because of ASGM, averaging 1,000 tons per annum from at least 70 different countries." This results primarily from the process known as amalgamation that involves the addition of mercury compounds to gold containing ore. The cited reference describes: "A range of different amalgamation techniques with different degrees of Hg emission is used. Hg can be added before the milling process (amalgamation of whole ore) releasing a substantially greater amount of Hg than the more commonly used method of amalgamation of powder concentrates where Hg is added after milling." Thus mercury can be emitted into the ambient air and exposure to ASGM workers as well as nearby residents may result in medically important body burdens of mercury. (Kristensen AK et al. A review of mercury exposure among artisanal small-scale gold miners in developing countries. 2014 Int Arch Occup Environ Health 87:579-590)

**Friday, April 22, 2016****Question:**

What is the role of the compound 4-dimethylaminophenol (4-DMAP) in the treatment of cyanide poisoning related to fire smoke inhalation?

**Answer:**

4-DMAP is a nitrate based cyanide antidote that works by oxidizing hemoglobin to methemoglobin. This cyanide antidote is commonly used in Germany but is not generally found in the US. However, with the advent of the use of hydroxycobalamin, methemoglobin-forming agents are no longer as commonly used in the treatment of smoke inhalation related presumptive cyanide poisoning as in the past. In addition, according to the cited reference, "4-DMAP administration may, however, be dangerous as it can cause tissue necrosis or phlebitis at the site of injection and nephrotoxicity....." (Mintegi S et al. Pediatric cyanide poisoning by fore smoke inhalation- A European expert consensus. 2013 Pediatr Emer Care 29:1234-1240)

**Thursday, April 21, 2016****Question:**

What is phytophotodermatitis? What compounds found in which materials are most commonly implicated in the development of this problem? What are the primary challenges with regard to correctly diagnosing phytophotodermatitis?

**Answer:**

The cited reference reports: "Phytophotodermatitis is a cutaneous eruption that occurs as a result of contact with photosensitizing compounds in plants and exposure to sunlight (especially ultraviolet A rays, 320-400 nm). These authors go on to state: "Furocou-marins found in limes, lemons, oranges, celery, figs, parsnips, parsley, carrots, pine lumber, and perfumes are commonly implicated". In addition, the authors of the cited reference state: "Diagnosis is sometimes difficult because erythema and vesicles in phytophotodermatitis may mimic atopic dermatitis, type IV hypersensitivity reaction, or chemical burns". (Abali A et al. Burns or phytophotodermatitis, abuse or neglect: Confusing aspects of skin lesions caused by the superstitious use of fig leaves. 2012 J Burn Care & Res. 33:e309-e312)

**Wednesday, April 20, 2016****Question:**

Occupational asthma may be caused by a specific sensitizer chemical found in the workplace. Such sensitizers are agents that induce asthma via mechanisms associated with a specific immunologic response. What characterizes occupational sensitizers?

**Answer:**

According to the cited reference: "Occupational sensitizers are commonly high-molecular- weight agents (>10 kD, usually a protein or glycopeptide) that can cause production of specific IgE antibodies and typical allergic responses. Once a person is sensi- tized, very low exposures can induce asthma, which s often associated with rhinoconjunctivitis. New causative agnets are reported each year and it would appear that almost any protein that becomes airborne and inhaled might be a potential cause of occupational asthma." (Tarlo SM and Lemiere C. Occupational asthma. 2014 NEJM 370: 640-649)

**Tuesday, April 19, 2016****Question:**

What are the manifestations of the so-called reversible cerebral vasoconstriction syndrome (RCVS) and which drugs have been associated with this syndrome?

**Answer:**

The cited reference notes that the clinical manifestations of RCVS include "recurrent sudden-onset and severe (thunderclap) headaches over 1-3 weeks, often accompanied by nausea, vomiting, photophobia, confusion and blurred vision." The authors go on to point out that " The major complications are localized convexity non-aneurysmal subarachnoid hemorrhage (22%) and ischemic stroke or intracerebral hemorrhage (7%) which may leave permanent residual neurological deficits." This syndrome, also known as "drug-induced cerebral arteritis" has been associated cocaine and other drugs that might exert sympathomimetic effects. (Sattar A et al. Systematic review of reversible cerebral vasoconstriction syndrome. 2010 Expert Rev Cardiovasc Ther 8(10): 1417-1421)

**Monday, April 18, 2016****Question:**

What is the HAART-associated lipodystrophy syndrome (HALS)?

**Answer:**

The cited reference describes: "The commonly observed adverse effects of HAART vary among treatment regimens and include gastrointestinal symptoms, hepatotoxicity, rash, and metabolic abnormalities associated with lipodystrophy. These abnormalities include significant increases in circulating low-density lipoprotein (LDL) and total cholesterol, triglycerides, and glucose levels, as well as decreased high-density lipoprotein (HDL) cholesterol levels. The combination of lipodystrophy and metabolic syndrome, or more specifically and more commonly dyslipidemia and impaired glucose tolerance in these patients, is defined as HIV/ HAART-associated lipodystrophy syndrome (HALS)." (Paruthi J et al. Adipokines in the HIV/HAART-associated lipodystrophy syndrome. 2013 Metabolism Clin Exp 62:1199-1205)

**Friday, April 15, 2016****Question:**

Which heavy metal has been noted by FDA to be of concern as an environmental contaminant in some infant rice cereal?

**Answer:**

The FDA notes: "Rice has higher levels of inorganic arsenic than other foods, in part because as rice plants grow, the plant and grain tend to absorb arsenic from the environment more than other crops. Arsenic is not intentionally added to rice grain, and when present in the grain, cannot be completely removed."

The FDA further states: "Based on its testing, the FDA on April 1, 2016 proposed an action level, or limit, of 100 parts per billion (ppb) for inorganic arsenic in infant rice cereal. This level, which is based on the FDA's assessment of a large body of scientific information, seeks to reduce infant exposure to inorganic arsenic. Relative to body weight, rice intake for infants, primarily through infant rice cereal, is about three times greater than for adults." ( <http://www.fda.gov/Food/FoodborneIllnessContaminants/Metals/ucm367263.htm>; accessed April 2016)

**Thursday, April 14, 2016****Question:**

Metronidazole-induced encephalopathy has been reported but is decidedly a rare disorder. What is the typical clinical presentation and natural course for this disorder and what are the characteristic MRI findings?

**Answer:**

According to the cited reference "The patient with metronidazole-induced encephalopathy typically presents with subacute progression of cognitive impairments and cerebellar ataxia which are resolved dramatically by discontinuation of treatment." The authors of the cited paper go on to describe: "....the most common [MRI] lesions were typically identified in the dentate nucleus, followed by corpus callosum, midbrain, basal ganglia, and subcortical white matter, all of which were usually symmetrical." (Furukawa S. et al. Metronidazole-induced encephalopathy with contrast enhancing lesions on MRI [Letter to the Editor] 2015 J Neurol Sci 352:129-131. See also Farmakiotis D and Zeluff B. Metronidazole-associated encephalopathy. 2015 NEJM 374:1465)

**Wednesday, April 13, 2016****Question:**

Why should oil based laxatives be avoided in the management of individuals who are transporting illicit drugs as "body packers"?



**Answer:**

The cited reference notes, since latex products are often used to wrap drugs concealed in body cavities, “The use of oil-based laxatives, although occasionally recommended, should be avoided because they reduce the tensile strength and “burst” volume of latex products.” (White N et al. Dangers of lubricants used with condoms. 1988 Nature 335:19 as cited in Traub SJ, Hoffman RS and Nelson LS. Body packing-The internal concealment of illicit drugs. 2003 NEJM 349:2519-2526)

**Tuesday, April 12, 2016****Question:**

Polymers of polyacrylonitrile are found in a wide variety of household products and textiles. The thermal combustion of the chemical polyacrylonitrile produces potentially lethal concentrations of what harmful substance?

**Answer:**

The thermal combustion of the chemical polyacrylonitrile produces potentially lethal concentration of hydrogen cyanide. This is the source of cyanide toxicity that often plays a role in the death of smoke inhalation victims. (Baud F et al. Elevated blood cyanide concentrations in victims of smoke inhalation. 1991 NEJM 325:1761-1766)

**Monday, April 11, 2016****Question:**

Chemotherapy-induced vomiting is a serious problem that can be stratified into five distinct categories. What are the five recognized categories of chemotherapy-induced vomiting?

**Answer:**

The cited reference notes five categories of chemotherapy-induced vomiting as follows.

1) “Acute”: “Occurring within the first 24 hours after initiation of chemotherapy, generally peaks after 5-6 hours”; 2) “Delayed”: “Occurring from 24 hours to several days after chemotherapy”; 3) “Breakthrough”: “Occurring despite appropriate prophylactic treatment”; 4) “Anticipatory”: “Occurring before a treatment as a conditioned response to the occurrence of chemotherapy induced nausea and vomiting in previous cycles”; 5) “Refractory”: “Recurring in subsequent cycles of therapy, excluding anticipatory chemotherapy-induced nausea and vomiting”. (Navari RM and Aapro M. Antiemetic prophylaxis for chemotherapy-induced nausea and vomiting. 2016 NEJM 374:1356-1367)

**Friday, April 8, 2016****Question:**

*Apis mellifera scutellata* (Africanized bees) are a very aggressive species known to inflict massive stinging attacks to victims. Acute kidney injury has been documented to complicate these attacks with more than 45 cases reported in the literature. What is the pathophysiology of renal failure secondary to massive bee stings inflicted by so-called Africanized bees?

**Answer:**

The cited reference notes “The pathophysiology of renal failure is related to direct nephrotoxicity from bee venom and this includes rhabdomyolysis, hemolysis and renal ischemia by anaphylaxis, hypervolemia or low cardiac output.” The authors further point out “. . .bee venom contains peptides such as melittin and phospholipase A which can provoke rhabdomyolysis and hemolysis. They have cytolytic effects that act on the phospholipid membranes of blood cells, muscles and the vascular endothelium, producing proinflammatory substances and hepatocellular lesions.” (Bridi RA et al. Acute kidney injury after massive attack of Africanized bees. 2014 BMJ Case Rep 2014. doi:10.1136/bcr-2013-201381)

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**Thursday, April 7, 2016****Question:**

The agent known as British anti-lewisite (BAL) has been recommended as a potential antidote against the arsenical agent lewisite (dichloro[2-chlorovinyl]arsine). What substance is this drug suspended in?

**Answer:**

BAL is suspended in peanut oil and thus it has been suggested BAL not be used in individuals with known peanut allergy. (Kosnett MJ. The role of chelation in the treatment of arsenic and mercury poisoning. 2013 J Med Toxicol 9:347-354)

**Wednesday, April 6, 2016****Question:**

The folic acid antagonists aminopterin and methotrexate have been used as abortifacients. Methotrexate continues to be used as an abortifacient whereas aminopterin is no longer used. Inadvertent or intentional prenatal exposure to folic acid antagonists in early pregnancy may lead to fetal death or to a dose-dependent pattern of malformations in liveborn infants. What characterizes the so-called fetal aminopterin/methotrexate syndrome?

**Answer:**

The fetal aminopterin/methotrexate syndrome may include microcephaly, severe hypoplasia of frontal, parietal, temporal or occipital bones, broad nasal bridge, prominent eyes, micrognathia, low set ears, and epicanthal folds among other problems. In addition cleft palate and neural tube defects have been reported. Mental and motor performance is usually normal. (Aftimos S. fetal methotrexate/aminopterin syndrome in an adult: a likely case with ectodermal abnormalities. 2009 Clin Dysmorphology 18:53-55)

**Tuesday, April 5, 2016****Question:**

It is often difficult to determine which patients feign pain in order to obtain opioid prescriptions from prescribers both in the office setting and in the emergency department. What percent of opioid drug diversion results from patients who feign pain in order to acquire prescriptions for these drugs?

**Answer:**

According to the cited reference, “Approximately 7-10% of diversion occurs among patients who feign pain to acquire prescribed opioids.” (Volkow ND and McLellan T. Opioid abuse in chronic pain-misconceptions and mitigation strategies. 2016 NEJM 374(13): 1253-1263)

**Monday, April 4, 2016****Question:**

Where in the human brain are the mu opioid receptors located?

**Answer:**

According to the cited reference, the mu opioid receptors are located in “high concentration in the thalamus, peri-aqueductal gray area, insula, and anterior cingulate, on the ventral tegmental area and nucleus accumbens, in the amygdala and in the brain stem”. (Volkow ND and McLellan T. Opioid abuse in chronic pain-misconceptions and mitigation strategies. 2016 NEJM 374(13): 1253-1263)

**Friday, April 1, 2016****Question:**

What is the clinical course of acute methyl bromide toxicity?

**Answer:**

The cited reference defined three phases in the clinical course of acute methyl bromide toxicity as follows: “a premonitory phase up to 48 h after exposure, with dimness of vision, diplopia, staggering gait, headache, vertigo, vomiting, euphoria or delirium, or syncope. The phase of cerebral irritation produces seizures, myoclonus, twitching, diaphoresis, and respiratory failure. If the patient survives, the recovery phase ensues.” (Wyers H. Methyl bromide intoxication. Br J Ind Med 1945; 2(1): 24–29 as cited in de Souza A, et al. The neurological effects of methyl bromide intoxication. 2013 J Neurol Sci 335:36-41)

**Thursday, March 31, 2016****Question:**

What is the likely pathophysiology of vancomycin-related “red man syndrome” (RMS)?

**Answer:**

According to the cited reference: “RMS is believed to be an anaphylactoid type of reaction due to vancomycin-induced direct mast cell degranulation. It has been shown to be associated with a rise in blood histamine level in some studies, however conflicting data exist. Increasing evidence suggests that altered histamine metabolism may contribute to the pathogenesis of hypersensitivity reactions including RMS.” (Myers AL et al. Defining risk factors for red man syndrome in children and adults. 2013 Pediatr Infect Dis 31:464-468)

**Wednesday, March 30, 2016****Question:**

What is the common name for the plant *Convallaria majalis*? This plant contains nearly 20 glycoside compounds including convallatoxin which is primarily responsible for potentially severe digitalis-like effects that may occur if this plant is ingested.

**Answer:**

Lily of the Valley. (Alexandre J, et al. Digitalis intoxication induced by an acute accidental poisoning by Lily of the Valley. 2012 Circulation 125:1053-1055)

**Tuesday, March 29, 2016****Question:**

What are the risks associated with broken metal halide light bulbs?

**Answer:**

According to the cited reference: “Metal halide lamps produce an electric arc that travels through a mixture of mercury and metal halide gases, generating an intense white light. Commonly used for overhead lighting, each lamp has a coated outer glass bulb surrounding the arc tube, which serves to filter out ultraviolet light. Broken metal halide lamps pose a risk for photokeratitis among exposed persons. In the first cluster reported, 242 persons developed photokeratitis following exposure to a single compromised metal halide bulb, and in the second, as few as 30 minutes of exposure to a metal halide bulb with a broken outer envelope resulted in 20 photokeratitis cases.” ( <http://www.cdc.gov/mmwr/volumes/65/wr/mm6511a4.htm>; accessed March 2016)

**Monday, March 28, 2016****Question:**

A recent controversy regarding products sold at Lumber Liquidators® stores in the US has been reported in the lay press. What are the issues that have been discussed with regard to this situation?

**Answer:**

The U.S. Consumer Product Safety Commission (CPSC) tested formaldehyde levels released from specific types of laminate flooring made in China between 2012 and 2014 and sold at Lumber Liquidators® stores in the United States. CPSC tested the same type of flooring that had some of the highest formaldehyde levels in tests conducted during a recent consumer investigation.

The Centers for Disease Control and Prevention (CDC) and the Agency for Toxic Substances and Disease Registry (ATSDR) estimated (modeled) indoor formaldehyde levels that may be present in typical homes with this laminate flooring. In the model, near worst-case conditions were used so that conclusions and recommendations would be aimed at protecting the public health. ( <http://www.cdc.gov/ncet/laminatelflooring/default.html>; accessed March 2016)

**Friday, March 25, 2016****Question:**

What is the main psychoactive alkaloid contained in the plant known as Kratom (*Mitragyna Speciosa*)?

**Answer:**

The primary psychoactive alkaloid in Kratom is mitragynine. (Singh D. et al. Kratom dependence, withdrawal symptoms and craving in regular users. 2014 Drug Alc Dependence 139:132-137)

**Thursday, March 24, 2016**

**Question:**

What toxicity is associated with exposure to the chemical 2-butoxy ethanol?

**Answer:**

Also known as butyl "cellosolve", 2-butoxy ethanol a glycol ether with surfactant properties, has been used as a component of fracturing fluids in the hydraulic fracturing process in the petroleum industry. 2-butoxy ethanol readily penetrates human skin and this route for absorption may account for a greater degree of absorption than does inhalation. Ocular exposure may result in eye pain, irritative symptoms and corneal damage. Animal models have demonstrated an increase in red blood cell fragility with hemolysis. ( <http://www.cdc.gov/niosh/docs/81-123/pdfs/0070.pdf>; accessed March 2016)

**Wednesday, March 23, 2016**

**Question:**

What is the Navajo Birth Cohort Study (NBCS)?

**Answer:**

The Navajo Birth Cohort Study (NBCS) is: "A prospective birth cohort study involving environmental uranium exposure in the Navajo Nation" is the first prospective epidemiologic study of pregnancy and neonatal outcomes in a uranium-exposed population. The Navajo Nation encompasses 16 million acres of New Mexico, Utah and Arizona, and is the largest Alaska Native / American Indian Reservation in the United States. From 1944 to 1986, hundreds of uranium mining and milling operations were conducted in the Navajo Nation. These mining and processing operations have left a legacy of potential uranium exposure through abandoned uranium mines/mills, drinking water and soil contamination, and homes and structures built with mining waste. The Navajo Nation central government is headquartered in Window Rock, Navajo Nation (Arizona). The goal of the NBCS is to better understand the relationship between uranium exposures and birth outcomes and early developmental delays on the Navajo Nation. ( [http://www.atsdr.cdc.gov/sites/navajo\\_birth\\_cohort\\_study/](http://www.atsdr.cdc.gov/sites/navajo_birth_cohort_study/); accessed March 2016)

**Tuesday, March 22, 2016**

**Question:**

Acetylfentanyl is a fentanyl analog whose physical appearance and pharmacologic action mimics heroin. What is the mechanism of action for this drug?

**Answer:**

The cited reference notes that acetylfentanyl "acts in the human body by agonism at the mu-opioid receptor, where its activity is 15.7 times more potent than morphine and 3 times less potent than fentanyl." (Rogers JS et al. Acetylfentanyl: An emerging drug of abuse. 2016 J Emerg Med 50(3): 433-436)

**Monday, March 21, 2016**

**Question:**

Which inhaled industrial toxicant, with a "garlicky odor", is the likely culprit when exposed individuals exhibit both a red/bronze tint of the skin and black or brown urine?

**Answer:**

Arsine. The cited reference notes: "Renal failure due to tubular destruction is an important sequelae of arsine exposure. Hemoglobin in the urine is thought to be the cause. Urinalysis typically shows large amounts of protein and free hemoglobin with only a few red blood cells. The urine is frequently discolored- brown, red or black. The characteristic red/bronze tint of the skin is induced by hemolysis and may be caused by hemoglobin deposits." Pullen-James and Woods SE. Occupational arsine gas exposure. 2006 J National Med Assoc 298(12):1998-2001)

**Friday, March 18, 2016**

**Question:**

Hydralazine induced lupus syndrome occurs in 5-10% of persons taking this drug. What are the clinical characteristics of this syndrome?

**Answer:**

Hydralazine-induced lupus syndrome presents with arthralgias, myalgias, fever and serositis. In some cases severe cardiac involvement has been reported but is quite rare. (Chamsi-Pasha M et al. Hydralazine-induced lupus syndrome presenting with large pericardial effusion. 2014 QJ Med 107:305-307)

**Thursday, March 17, 2016**

**Question:**

What is heptachlor?

**Answer:**

Heptachlor is a manufactured chemical and doesn't occur naturally. Pure heptachlor is a white powder that smells like camphor (mothballs). The less pure grade is tan. Trade names include Heptagran®, Basaklor®, Drinox®, Soleptax®, Termide®, and Velsicol 104®. Heptachlor was used extensively in the past for killing insects in homes, buildings, and on food crops, especially corn. These uses stopped in 1988. Currently it can only be used for fire ant control in power transformers. Heptachlor epoxide is also a white powder. Bacteria and animals break down heptachlor to form heptachlor epoxide. The epoxide is more likely to be found in the environment than heptachlor. ( <http://www.atsdr.cdc.gov/toxfaqs/tf.asp?id=744&tid=135>; accessed February 2016)

**Wednesday, March 16, 2016**

**Question:**

What is Micotil 300 and what health hazards are of concern in humans who handle this material?

**Answer:**

Micotil 300 is the trade name for the chemical tilmicosin phosphate, an animal antibiotic used to treat "shipping fever", a bovine and ovine respiratory disease. In the U.S., veterinarians give Micotil 300 to animals but more frequently prescribe it for their clients to use on cattle and sheep at livestock facilities. Micotil 300 may enter the body via skin puncture and its primary adverse effects involve cardiotoxicity including reduced cardiac contractility and tachycardia. Deaths have been reported, usually associated with suicidal gestures. ( [www.cdc.gov/niosh/docs/wp-solutions/2007-124/pdfs/2007-124.pdf](http://www.cdc.gov/niosh/docs/wp-solutions/2007-124/pdfs/2007-124.pdf); accessed March 2016)

**Tuesday, March 15, 2016**

**Question:**

What is tetryl?

**Answer:**

The chemical name for tetryl is 2,4,6-trinitrophenyl-n-methylnitramine. Some commonly used names are nitramine, tetralite, and tetril. Tetryl is an odorless, synthetic, yellow crystal-like solid that is not found naturally in the environment. Under certain conditions, tetryl can exist as dust in air. It dissolves slightly in water and in other liquids. Tetryl was used to make explosives, mostly during World Wars I and II. It is no longer manufactured or used in the United States. Stocks of tetryl are found in storage at military installations and are being destroyed by the Department of Defense (DOD). According to the cited reference, "Exposure to tetryl occurs around military installations where it was made, used, or stored. Workers who breathed tetryl-laden dust complained of coughs, fatigue, headaches, eye irritation, lack of appetite, nosebleeds, nausea, and vomiting." ( <http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=216>; accessed March 2016)

**Monday, March 14, 2016**

**Question:**

When heroin users develop asymptomatic proteinuria and nephrotic syndrome which specific renal disorder, that may require renal biopsy for diagnosis, should be considered?

**Answer:**

Renal amyloidosis should be considered in heroin users with asymptomatic proteinuria and nephrotic syndrome. (Cooper C et al. Serum amyloid A renal amyloidosis in a chronic subcutaneous ("skin popping") heroin user. 2013 J Nephropathology 2(3): 196-200)

**Friday, March 11, 2016****Question:**

What is the pathophysiology of cadmium induced nephropathy?

**Answer:**

Roughly 30% of absorbed cadmium is stored in the kidneys, where it persists with a biologic half-life of up to 30 years. The cited reference notes: "In chronic cadmium exposure much of the plasma cadmium is bound to metallothionein (MT). Due to its small molecular size, cadmium-MT, in contrast to the cadmium-albumin complex, is efficiently filtered through the glomerular membrane and reabsorbed by renal tubular cells through pinocytosis. The cadmium-MT complex is then metabolized within lysosomes and cadmium ion is released. Cadmium nephropathy presents as tubular proteinuria that can be quantified by measuring low molecular weight proteins including beta-2 microglobulin and retinol binding protein. With continued cadmium exposure this tubular dysfunction progresses and ultimately glomerular damage characterized by a decreased glomerular filtration rate may emerge. Several studies have documented that in almost all cases, this cadmium-induced tubular proteinuria and damage is irreversible even if exposure ends." (Wittman R and Hu H. Cadmium exposure and nephropathy in a 28-year-old female metals worker. 2002 Environ Health Perspect 110:1261-1266)

**Thursday, March 10, 2016****Question:**

Acute CNS toxicity occurs within hours following methotrexate administration, and may involve signs of chemical meningitis: somnolence, confusion, headache, nausea, vomiting, and dizziness. Subacute CNS toxicity is observed within days to weeks of methotrexate therapy, and patients may exhibit seizures or stroke-like signs including hemiparesis, hemisensory deficits, aphasia, dysarthria, dysphagia, and diplopia. Which non-competitive N-methyl-D-aspartate receptor antagonist has been used in the treatment of subacute neurological dysfunction associated with methotrexate toxicity?

**Answer:**

Although controversial, the cited review suggests that the non-competitive N-methyl-D-aspartate receptor antagonist dextromethorphan can be helpful in relieving symptoms associated with methotrexate toxicity. (Afshar M et al. Review of dextromethorphan administration in 18 patients with subacute methotrexate central nervous system toxicity. 2014 Pediatr Neurol 50:625-629)

**Wednesday, March 9, 2016****Question:**

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**Tuesday, March 8, 2016****Question:**

What is "MBOCA"?

**Answer:**

MBOCA is a synthetic chemical used primarily to make polyurethane products. Pure MBOCA is a colorless, crystalline solid, but the commonly used form is usually yellow, tan, or brown pellets. It has no smell or taste. Examples of these products include gears, gaskets, sport boots, roller skate wheels, shoe soles, rolls and belt drives in cameras, computers and copy machines, wheels and pulleys for escalators and elevators, components in home appliances, and various military applications. It is also used as a coating in chemical reactions to "set" glues, plastics, and adhesives. Because plastics have many uses, MBOCA is widely used. Other names for MBOCA include 4,4'-methylenebis(2-chloroaniline), methylene-bis-ortho-chloro-aniline, bis-amine, DACPM, MCA, and MOCA. ( <http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=209>; accessed February 2016)

**Monday, March 7, 2016****Question:**

What is QNB?

**Answer:**

"QNB" is 3-Quinuclidinyl benzilate, also known as "BZ" or "Agent Buzz", is an incapacitating agent and has been considered historically for use as a chemical warfare agent. The cited reference states "A very potent drug, QNB causes confusion and hallucinations and an anticholinergic toxidrome. Impairments caused by QNB are generally temporary and unlikely to be fatal; however, they can be severe if exposure is large enough." ( [http://www.cdc.gov/niosh/erashdb/emergencysresponsecard\\_29750015.html](http://www.cdc.gov/niosh/erashdb/emergencysresponsecard_29750015.html); accessed March 2016)

**Friday, March 4, 2016****Question:**

What is the so-called episome?

**Answer:**

Success in mapping the human genome has fostered the complementary concept of the "exposome". The exposome can be defined as the measure of all the exposures of an individual in a lifetime and how those exposures relate to health. An individual's exposure begins before birth and includes insults from environmental and occupational sources. Understanding how exposures from our environment, diet, lifestyle, etc. interact with our own unique characteristics such as genetics, physiology, and epigenetics impact our health is how the exposome will be articulated. Exposomics is the study of the exposome. ( <http://www.cdc.gov/niosh/topics/exposome/>; accessed February 2016)

**Thursday, March 3, 2016****Question:**

QT prolongation and occasionally torsades de pointes develops with some antipsychotic drugs. When ingested in intentional overdose, which antipsychotic drugs are associated with QT interval prolongation and increased risk for torsades de pointes?

**Answer:**

The authors of the cited study concluded: "There appeared to be significant risk of QT prolongation with amisulpride and thioridazine overdoses. Although there were abnormal QT intervals for quetiapine, olanzapine, and risperidone overdoses, they were associated with tachycardia and not dose dependent, and so were unlikely to be associated with increased torsades de pointes risk." (Berling I and Isbister GK. Prolonged QT risk assessment in antipsychotic overdose using the QT nomogram. 2015 Anns Emerg Med 66(2): 154-164)

**Wednesday, March 2, 2016**

**Question:**

What are the major sources of exposure to perfluoroalkyls including PFOA (perfluorooctanoic acid) and PFOS (perfluorooctane sulfonic acid)?

**Answer:**

Contaminated drinking water and contaminated food are the primary sources of exposure for perfluoroalkyls. However industrial releases of these chemicals into ambient air or surface water may also be important sources. The cited reference notes: "The general population may also be exposed to PFOS from mill treated carpets and to PFOA from migration from paper packaging and wrapping into food and inhalation from impregnated clothes." (ATSDR 2015. Toxicological Profile for Perfluoroalkyls (Draft for Public Comment) Atlanta Georgia: US Dept of HHS, PHS)

**Tuesday, March 1, 2016**

**Question:**

What is the role for inhaled anticoagulation regimens to manage smoke inhalation-associated acute lung injury?

**Answer:**

A recent systematic review reported: "The high mortality associated with smoke inhalation-associated acute lung injury results from airway damage, mucosal dysfunction, neutrophil infiltration, airway coagulopathy with cast formation, ventilation-perfusion mismatching with shunt, and barotrauma. Inhaled anticoagulation regimens in both preclinical and clinical studies improve survival and decrease morbidity without altering systemic markers of clotting and anticoagulation. In some preclinical and clinical studies, inhaled anticoagulant's were associated with a favorable effect on survival. This approach appears sufficiently promising to merit a well-designed prospective study to validate its use in patients with severe smoke inhalation-associated acute lung injury requiring mechanical ventilation." (Miller AC et al. Inhaled anticoagulation regimens for the treatment of smoke inhalation-associated acute lung injury: A systematic review. 2014 Crit Care Med 42(2): 413-419)

**Monday, February 29, 2016**

**Question:**

The safety of using the serotonin 5-HT<sub>3</sub> receptor antagonist, ondansetron, as an antiemetic during pregnancy has been debated. Some large studies have reported no increased risk for adverse fetal outcomes. Which notable teratogenic risk has been reported as a result of ondansetron use in pregnancy?

**Answer:**

The cited study evaluated more than 1.5 million infants with regard to pre-natal ondansetron exposure and reported: "The risks for a cardio-vascular defect and notably a cardiac septum defect were increased and statistically significant (OR=1.62, 95% CI 1.04-2.14 and RR 2.05, 95% CI 1.19-3.28, respectively). The teratogenic risk with ondansetron is low but an increased risk for a cardiac septum defect is likely." (Danielsson B et al. Use of ondansetron during pregnancy and congenital malformations in the infant. 2014 Reproductive Tox 50: 134-137)

**Friday, February 26, 2016**

**Question:**

Virtually all solid organ transplant recipients (80-98%) receive the drug tacrolimus at some point in their post-transplant course. The most commonly recognized adverse effects of this drug include hyperglycemia, nephrotoxicity and neurotoxicity. What other major organ system toxicity has been associated with the use of tacrolimus?

**Answer:**

Tacrolimus has been responsible for the development of significant cardiomyopathy. The cited reference states "The cardiotoxic effects of tacrolimus have been most commonly characterized as obstructive or concentric hypertrophic cardiomyopathy and primarily described in pediatric transplant recipients. Although the mechanism of tacrolimus-induced cardiomyopathy (TICM) has not been fully elucidated, theories exist. The pathogenesis of TICM may be secondary to the binding of tacrolimus to FK506 binding proteins (FKBP) in cardiac muscle." (Bowman LJ et al. Tacrolimus-induced cardiomyopathy in an adult renal transplant recipient. 2015 Pharmacotherapy 35(12): 1109-1116)

**Thursday, February 25, 2016**

**Question:**

Tarantulas are popular pets. While these creatures do not inflict injury with a toxin, they can inflict injury due to their defensive hairs, typically located on the animal's abdomen. What characterizes ocular injury from these hairs and what is the most appropriate treatment?

**Answer:**

The cited reference notes: "Common presenting symptoms of ocular injury from tarantula hairs include conjunctival injection, foreign body sensation, periorbital facial rash, photophobia, and tearing. Because many of these symptoms are similar to other diagnoses, the presence of ocular injury secondary to tarantula hairs can be initially difficult to detect. Slit-lamp examination reveals hairs that can be either light or dark in color, and their description varies, from 'clear, acrylic rods' to dark and 'resembling needles'."

These authors also point out: "After diagnosis of tarantula hair ocular injury, the first decision to be made in terms of treatment is whether removal of the hairs should be attempted. Some reports suggest better outcomes if the hairs can be removed. However, removal of the hairs is not appropriate in all cases. Factors that suggest leaving the hairs include: a large number of hairs, deep corneal penetration, lack of patient tolerance, and risk of perforation. It has been suggested that the removal of deeper hairs is not necessary because the hairs may be absorbed without further complications." (Stagg BC and Ambatai BK. Tarantula hairs as corneal foreign bodies. 2011 Case Rep in Ophthalmol 2:323-326)

**Wednesday, February 24, 2016**

**Question:**

What are mineral-based crankcase oils?

**Answer:**

The cited reference notes "Mineral-based crankcase oils are manufactured using highly refined base oils and contain up to 20% of a variety of additives such as viscosity index improvers, detergents/dispersants, antiwear additives, pour-point depressants, and antioxidants. During use, the high temperatures and friction cause changes such as oxidation, nitration, and cracking of polymers in the component chemicals. In addition, a variety of substances such as fuel, water, antifreeze, dust, and various combustion products such as polycyclic aromatic hydrocarbons (PAHs), metals, and metallic oxides accumulate in the oil. The degree of chemical change and accumulation of contaminants in the oil increases with use and varies depending on the type of fuel used and the mechanical properties of the engine."

Mineral-based crankcase oils pose a potential threat to ground water and the environment when improperly disposed of.  
( <http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=123>; accessed January 2016)

**Tuesday, February 23, 2016**

**Question:**

Tick paralysis results from the secretion of a neurotoxin and is not an infectious disease. Which species of tick have been associated with the development of tick paralysis in humans and how long after initial attachment does this paralysis usually have its onset?

**Answer:**

A number of tick species have been associated with the development of paralysis in humans including Dermacentor, Amblyomma and Ixodes. According to the cited reference, paralysis usually begins within 48 hours to 6 days following attachment of the tick. (Pecina CA Tick paralysis. 2012 Semin Neurol 32(5): 531-532 and Green WL and Millsap WG Tick-borne illness. 2016 Crit Dec in Emerg Med 30(1):3-9)

**Monday, February 22, 2016**

**Question:**

Tick bites can sensitize patients to a specific food with possible subsequent generalized urticaria and/or anaphylaxis. What is the food and what is the mechanism of sensitization?

**Answer:**

According to the cited reference, tick bites can result in sensitization to red meat. The mechanism involves a human reaction to the oligosaccharide galactose- $\alpha$ -1,3-galactose present in both ticks and non-primate mammalian meat (e.g. beef, pork, lamb). (Commins SP et al The relevance of tick bites to the production of IgE antibodies to the mammalian oligosaccharide galactose- $\alpha$ -1,3-galactose. 2011 J Allergy Clin Immunol 127(5):1286-1293 and Green WL and Millsap WG. Tick Borne Illness. 2016 Crit Dec in Emerg Med 30(1):3-9)

**Friday, February 19, 2016****Question:**

Beta blockers are commonly used as antihypertensive drugs in pregnancy and most beta blocker drugs are classified as FDA class C (i.e. animal studies have shown adverse fetal effects but there are no adequate or well controlled studies in humans but potential benefits may warrant use in pregnancy despite potential risks). What is the risk for congenital malformations associated with exposure to beta blockers in early pregnancy?

**Answer:**

The cited reference reported a recently published meta-analysis aimed to determine the teratogenicity of  $\beta$ -blockers in early pregnancy. According to this study: “first-trimester oral  $\beta$ -blocker use showed no increased odds of all or major congenital anomalies (OR=1.00; 95% confidence interval, 0.91–1.10; 5 studies). However, in analyses examining organ-specific malformations, increased odds of cardiovascular defects (OR=2.01; 95% confidence interval, 1.18–3.42; 4 studies), cleft lip/palate (OR=3.11; 95% confidence interval, 1.79–5.43; 2 studies), and neural tube defects (OR=3.56; 95% confidence interval, 1.19–10.67; 2 studies) were observed. The effects on severe hypospadias were nonsignificant (1 study). Causality is difficult to interpret given the small number of heterogeneous studies and possibility of biases. Given the frequency of this exposure in pregnancy, further research is needed.” (Yakoob MY et al. The risk of congenital malformations associated with exposure to  $\beta$ -blockers early in pregnancy a meta-analysis. 2013 Hypertension 62:375-381)

**Thursday, February 18, 2016****Question:**

Statin drugs are known to cause myopathy however in the vast majority of cases this myopathy is relatively mild. Rarely, (2-3 of every 100,000 treated patients), statins have been associated with the development of a true autoimmune myopathy. What characterizes this autoimmune myopathy due to statin drugs?

**Answer:**

According to the cited reference, statin-associated autoimmune myopathy is characterized by “muscle weakness, evidence of muscle cell necrosis on biopsy, and the presence of autoantibodies against 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase”. These patients usually present with symmetrical proximal muscle weakness and persistently elevated creatine kinase levels in excess of 2000 IU per liter. The author of the cited reference further notes: “In contrast to most patients who have side effects from statin therapy, those with statin-associated autoimmune myopathy may have progressive weakness that must be controlled with immunosuppressive therapy.” (Mammen AL. Statin-associated autoimmune myopathy. 2016 NEJM 374(7): 664-669)

**Wednesday, February 17, 2016****Question:**

Which chemicals are commonly included in the group designated as phosphate ester flame retardants?

**Answer:**

The following chemicals are commonly included in the group designated as phosphate ester flame retardants: tris(2-chloroethyl) phosphate (TCEP), tributyl phosphate (TnBP), tris(2-butoxyethyl) phosphate (TBEP), tris(1,3-dichloro-2-propyl) phosphate (TDCP), triphenyl phosphate (TPP), tris(2-chloroisopropyl) phosphate (TCPP), triisobutyl phosphate (TiBP), and tricresyl phosphate (TCP). (<http://www.atsdr.cdc.gov/toxprofiles/tp202.pdf>; accessed February 2016)

**Monday, February 15, 2016****Question:**

What are the usual organotin compounds and what are their common uses?

**Answer:**

According to the cited reference: “Tin can combine with carbon to form organotin compounds (i.e., dibutyltin, tributyltin, triphenyltin). These compounds are used to make plastics, food packages, plastic pipes, pesticides, paints, and pest repellents.” ( <http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=98>; accessed January 2016)

**Friday, February 12, 2016****Question:**

The epidemic use of opioids is widely discussed with regard to prescription opioids. However the use of raw opium is also widespread and has been estimated to be used by at least four million people worldwide. The use of raw opium has been associated with the development of which forms of cancer?

**Answer:**

According to the cited systematic review, “Opium use was associated with an increased risk of cancers of the oesophagus, stomach, larynx, lung, and urinary bladder.” These authors point out “Although the present evidence suggests that these associations are possibly causal, further epidemiological studies (particularly prospective studies that collect detailed data about lifetime opium use and control for a broad range of potential confounders) are needed.” (Kamangar F. et al. Opium use: an emerging risk for cancer. 2014 Lancet Oncol 15: e69-77)

**Thursday, February 11, 2016****Question:**

What are so-called “AWOL” devices?

**Answer:**

“AWOL” devices are “alcohol without liquid devices”; basically nebulizers that aerosolize alcohol into an inhalable mist to allow for alcohol (ethanol) use via inhaling rather than drinking it. According to the cited reference, “It is advertised that users can feel the effects of alcohol with fewer calories and no hangovers. However these claims have not been substantiated. Although alcohol inhalation may not raise the blood alcohol level to the intoxication threshold, there is a rapid increase in blood alcohol levels. Adverse effects are unknown and require further investigation. (LeFoll B and Loheswaran G. Alcohol inhalation. 2014 CMAJ 186 (10): E399-E399)

**Wednesday, February 10, 2016****Question:**

What characterizes so-called aspirin-exacerbated respiratory disease (AERD)?

**Answer:**

The cited reference notes “aspirin-exacerbated respiratory disease (AERD) is characterized by asthma, chronic rhinosinusitis with nasal polyposis and pathognomonic respiratory reactions to aspirin (Samters triad).” These authors further note “it has been estimated that this syndrome affects 7% of adults with asthma and 14% of those who have severe asthma.” (Laidlaw TM and Boyve J. Aspirin exacerbated respiratory disease- new prime suspects. 2016 NEJM 374 95): 484-488)

**Tuesday, February 9, 2016****Question:**

What are the potential renal injuries that may occur after acute, high dose lead exposure?

**Answer:**

According to the cited reference, “Renal injury that appears after acute high-dose lead exposure may include reversible deficits in proximal tubular reabsorption and pre-renal azotemia induced by renal vasoconstriction and/or volume depletion.” (Kosnett MJ et al. Recommendations for medical management of adult lead exposure. 2007 Env Health Perspectives 115(3): 463-471)

**Monday, February 8, 2016****Question:**

When is the best time to assess alcohol consumption and inform women about health consequences to them and their children?

**Answer:**

The cited reference points out that approximately 50% of all pregnancies in the United States are unplanned, and alcohol-related fetal harm can occur in early pregnancy, before a woman recognizes that she is pregnant. Therefore, the best time to assess alcohol consumption and inform women about health consequences to them and their child is before pregnancy. (MMWR. Vital signs: Alcohol exposed pregnancies- United States, 2011-2013. February 5, 2016 65(4): 91-97)

**Friday, February 5, 2016****Question:**

Ototoxicity is a known complication related to aminoglycoside antibiotics. What is the effect of the co-administration of N-acetylcysteine (NAC) with regard to aminoglycoside induced ototoxicity?

**Answer:**

A recently published systematic review and meta-analysis reported: “Three studies reported that NAC reduced ototoxicity in 146 patients with end-stage renal failure receiving aminoglycosides. Pooled relative risk for otoprotection at 4–6 weeks was 0.14 (95% CI 0.05 to 0.45), and the risk difference was –33.3% (95% CI 45.5% to 21.2%). Eighty-three studies (N=9988) described the administration of NAC for >6 weeks. Abdominal pain, nausea and vomiting, diarrhea and arthralgia were increased 1.4–2.2 times.” These authors further stated “This review provides evidence for the safety and otoprotective effect of NAC when co-administered with aminoglycoside. It represents a strong justification for a clinical trial to investigate the effect of concomitant NAC treatment in patients receiving aminoglycosides..” (Kranzer K et al. A systematic review and meta-analysis of the efficacy and safety of N-acetylcysteine in preventing aminoglycoside-induced ototoxicity: implications for the treatment of multidrug-resistant TB. 2015 Thorax 70:1070-1077)

**Thursday, February 4, 2016****Question:**

What is the association, if any, between occupational lead exposure and amyotrophic lateral sclerosis (ALS)?

**Answer:**

According to a recently published meta-analysis, “The risk of developing ALS among individuals with a history of exposure to lead was almost doubled (odds ratio, 1.81; 95% confidence interval, 1.39 to 2.36) on the basis of nine included case-control studies with specific lead exposure information, with no apparent heterogeneity across included studies (I<sup>2</sup> = 14%). The attributable risk of ALS because of exposure to lead was estimated to be 5%.” The authors of this study concluded “Previous exposure to lead may be a risk factor for ALS.” They further noted “Confirmation of the present findings in future studies would serve both to elucidate the causes of ALS, and to support risk mitigation actions to further reduce the risk of ALS because of exposure to lead from occupational and other sources.” (Wang MD et al. A meta-analysis of observational studies of the association between chronic occupational exposure to lead and amyotrophic lateral sclerosis. 2014 JOEM 56(12): 1235-1242)

**Wednesday, February 3, 2016****Question:**

What are the factors thought to increase vulnerability to addiction?

**Answer:**

According to the cited reference: “Factors that increase vulnerability to addiction include family history (presumably through heritability and child-rearing practices), early exposure to drug use (adolescence is among the periods of greatest vulnerability to addiction), exposure to high-risk environments (typically, socially stressful environments with poor familial and social supports and restricted behavioral alternatives and environments in which there is easy access to drugs and permissive normative attitudes toward drug taking), and certain mental illnesses (e.g., mood disorders, attention deficit–hyperactivity disorder, psychoses, and anxiety disorders).” (Volkow ND et al. Neurobiologic advances from the brain disease model of addiction. 2016 NEJM 374:363-371)

**Tuesday, February 2, 2016****Question:**

Pregnancy complicated by depression may be associated with a variety of other complications, including preterm delivery, low birth weight, neonatal complications, and behaviors that may compromise the health of both mother and child. What are the maternal and fetal comparative benefits and risks of antidepressant treatment for depression in pregnant or postpartum women?

**Answer:**

A recently published systematic review and meta-analysis involving 6 randomized controlled trials and 15 observational studies concluded “Evidence about the comparative benefits and harms of pharmacologic treatment of depression in pregnant and postpartum women was largely inadequate to allow informed decisions about treatment. Considering the prevalence of depression, filling this gap is essential.” (McDonough MS et al. Depression drug treatment outcomes in pregnancy and the postpartum period. 2014 Obstet Gynecol 124:526-534)

**Monday, February 1, 2016****Question:**

Urine assays for thiodiglycolic acid (TDG) have been used in the occupational setting to assess for exposure to vinyl chloride. Why is TDG a relatively poor biomarker for vinyl chloride exposure?



**Answer:**

TDG is a relatively poor urine biomarker for exposure to vinyl chloride because it is not specific for VC exposure. TDG is often found as a normal constituent of non-exposed human urine and can also be found in the urine of individuals with hepatic disease as well as after alcohol use. (Mueller G et al. An analytical method using GC-MS for the quantitative determination of urinary thiodiglycolic acid. 1999 Int Arch Occup Env Health 44:185-191)

**Friday, January 29, 2016****Question:**

What is the so-called "Lead and Copper Rule" (LCR)?

**Answer:**

The LCR addresses the fact that lead and copper enter drinking water primarily through plumbing materials. In 1991, EPA published the LCR to minimize lead and copper in drinking water. The rule replaced the previous standard of 50 ppb, measured at the entry point to the distribution system. The rule established a maximum contaminant level goal (MCLG) of zero for lead in drinking water and a treatment technique to reduce corrosion of lead and copper within the distribution system. ( <http://www.epa.gov/dwreginfo/lead-and-copper-rule>; accessed January 2016)

**Thursday, January 28, 2016****Question:**

The Safe Drinking Water Act mandates the presentation of Consumer Confidence Reports (CCRs). What are CCRs?

**Answer:**

According to the EPA, A CCR is an annual water quality report delivered by community water systems to their customers. The CCR includes information on source water, the levels of detected contaminants, compliance with drinking water rules, and some educational language. The reports are due to customers by July 1st of each year. <http://www.epa.gov/ccr>; accessed January 2016)

**Wednesday, January 27, 2016****Question:**

In 2011, the U. S. Food and Drug Administration approved ruxolitinib, a potent immunosuppressive agent, for the treatment of intermediate and high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis. Which potentially life-threatening infections have been reported in patients who have received ruxolitinib?

**Answer:**

The potentially life threatening infections reported in patients who have received ruxolitinib include disseminated herpes simplex virus and viral progressive multifocal leukoencephalopathy. These infections may be due, in part, to ruxolitinib induced reduction in numbers of natural killer cells. (van Hofsten J et al. Cytomegalovirus retinitis in a patient who received ruxolitinib. 2016 NEJM 374:296-297)

**Tuesday, January 26, 2016****Question:**

What is apoptosis?

**Answer:**

The cited reference notes that apoptosis is "a normal mechanistic process in which cells that acquire or receive unrepairable severe damage to DNA or other cellular macromolecules, or cells with a low apoptotic threshold are selectively removed from the tissue." These authors go on to note: "With respect to carcinogenesis, it is generally accepted that cancer processes are balanced. Thus, the apoptotic process serves as a cellular mechanism to counter aberrant proliferation." (Klaunig JE et al. Epigenetic mechanism of chemical carcinogenesis. 2000 Human Exp Tox 19:543-555)

**Monday, January 25, 2016****Question:**

Should osteoporosis (anti-resorptive) therapy (e.g. bisphosphonates) be stopped prior to dental procedures?

**Answer:**

According to the cited reference: "The American Dental Association in 2011 recommended that osteoporosis therapy does not require alteration before dental procedures. A recent review suggested that before major, invasive dental surgery, consideration should be given to stopping antiresorptive therapy; the review also emphasized the importance of good dental hygiene in reducing risk." (Black DM and Rosen CJ. Postmenopausal osteoporosis. 2016 NEJM 374: 254-262 and Khan AA et al. Diagnosis and management of osteonecrosis of the jaw: a systematic review and international consensus. 2015 J Bone Miner Res 30:3-23)

**Friday, January 22, 2016****Question:**

Podophyllin is a mixture of resins derived from the rhizome and roots of Podophyllum emodi and Podophyllum peltatum (mayapple or American mandrake). Laryngeal papilloma, oral leukoplakia, and genital warts may be treated using podophyllin. What are the manifestations of local and systemic toxicity related to podophyllin?

**Answer:**

The cited reference states: "The active constituent of the toxin is podophyllotoxin, a lipid-soluble compound that readily crosses cell membranes. Local toxicity includes erythema, edema, chemical burns, and allergic sensitivity. Systemic toxicity (usually related to ingestion) includes nausea, vomiting, tachypnea, fever, stupor, coma, tachycardia, hypotension, paralytic ileus, renal failure, pancytopenia, peripheral neuropathy, and death.

The major concern with podophyllin poisoning is neurotoxicity. During the first day, toxic encephalopathy may manifest as altered mental status ranging from mild confusion to frank coma. Hallucinations and seizures can also occur." (Kumat M et al. Permanent neurological sequelae following accidental Podophyllin ingestion. 2012 J Child Neurol 27(2): 209-210)

**Thursday, January 21, 2016****Question:**

What is tungsten?

**Answer:**

The cited reference notes: "Tungsten is a naturally occurring element that, in most environments, is a solid. In nature, it occurs in rocks and soil as minerals, but never as the pure metal. Two kinds of tungsten-bearing mineral rocks, called wolframite and scheelite, are mined commercially. Elemental tungsten, like elemental copper or gold, is a metal. Tungsten can be used as a pure metal or mixed with other metals to make alloys that tend to be strong and flexible, resist wear, and conduct electricity well. Tungsten and its alloys are used as light bulb filaments, as the part of x-ray tubes where x-rays are formed, as a catalyst to speed up chemical reactions, as a component of steel in high-speed tools, in turbine blades, in phonographic needles, as welding electrodes, as gyroscope wheels, as counterbalance and fishing weights, in darts, and in golf club components. They can be used in bullets (as a replacement for lead) and in armor penetrators (as a substitute for depleted uranium). Chemical compounds of tungsten are used for many purposes. Cemented tungsten carbide, a hard substance used to make grinding wheels and cutting or forming tools, is the most common tungsten compound. Other tungsten compounds are used in ceramic pigments, as fire retardant coatings for fabrics, and as fade-resistant dyes for fabrics." ( <http://www.atsdr.cdc.gov/toxprofiles/tp186.pdf>; accessed January 2016)

**Wednesday, January 20, 2016**

**Question:**

Three clinical forms of anthrax have been identified: gastrointestinal, cutaneous and inhalational. Anthrax meningitis is a feared complication of clinical anthrax. What is the mechanism for the development of anthrax meningitis and which forms of anthrax are associated with the development of anthrax meningitis?

**Answer:**

According to the cited reference: "Anthrax meningitis, a result of hematogenous bacterial dissemination and meningeal seeding, can occur as a complication of all types of anthrax and has been noted in up to half of persons with inhalation anthrax cases. Anthrax meningitis is an expected complication during an anthrax mass-casualty incident. The impact of early combination intravenous antimicrobial therapy on the incidence of this complication is unknown. The clinical presentation of anthrax meningitis resembles that of other forms of bacterial meningitis. Symptoms include altered mental status, fever, headache, nausea/vomiting, seizures, focal neurologic deficits, and meningeal signs such as nuchal rigidity and the Kernig and Brudzinski signs." (Bower WA et al. Clinical framework and medical countermeasures use during an anthrax mass-casualty incident. MMWR December 4, 2015/ 64(RR04); 1-28

**Tuesday, January 19, 2016**

**Question:**

During the past 7 decades, at least 12 documented occurrences of diethylene glycol (DEG) contamination of medications have resulted in at least 450 deaths. Renal injury and neurological problems are the hallmark of severe poisoning with this substance. What is the presumed mechanism of injury causing the renal and neurological effects associated with DEG poisoning?

**Answer:**

According to the cited reference: "DEG is metabolized into 2 primary metabolites, 2- hydroxyethoxyacetic acid (2-HEAA) and diglycolic acid (DGA). Much of its toxicity is attributed to 2-HEAA. However one study suggested that the intracellular uptake of the other metabolite, DGA, is the cause of toxicity, particularly in the kidneys. A recent report on human samples from the Panama DEG mass poisoning has further implicated these 2 metabolites with the detection of 2-HEAA and DGA in the sera and DGA in the urine of cases. This was consistent with prior animal data. Interestingly, DGA and HEAA were significantly present in CSF samples of cases and not controls, which may be linked to the symptoms and signs of neurotoxicity. The exact mechanism of neurotoxicity, however, remains unknown." (Imam Y et al. Neurological manifestations of recreational fatal and near-fatal diethylene glycol poisonings. Medicine 2014 93(10): 1-8)

**Monday, January 18, 2016**

**Question:**

Poisoning with which substance must be considered if severe gastrointestinal symptoms and pancytopenia co-exist after ingestion of wild plants that may be used in salads, or to flavor drinks or sauces?

**Answer:**

According to the cited reference: "Colchicine poisoning should be considered in unexplained gastrointestinal symptoms and pancytopenia after ingestion of wild plants used to flavor sauces, drinks or salads." (Galland-Decker C et al. Progressive organ failure after ingestion of wild garlic juice. 2016 J Emerg Med 50(1): 55-60)

**Friday, January 15, 2016**

**Question:**

What is phosgene oxime?

**Answer:**

Phosgene oxime is a manufactured chemical that was developed as a potential chemical warfare agent, but its use on the battlefield has never been documented. It has a disagreeable penetrating odor. Pure phosgene oxime is a colorless, crystalline solid; the munitions grade compound is a yellowish-brown liquid. Both the liquid and the solid can give off vapors at ambient temperatures. Phosgene oxime produces instant and almost unbearable pain on exposed skin and exposed eyes. When inhaled, it causes immediate irritation to the respiratory (breathing) tract. Phosgene oxime can penetrate clothing and rubber faster than other chemical warfare agents. No antidote exists for phosgene oxime. Treatment consists of removing the phosgene oxime from the body as soon as possible and providing supportive medical care in a hospital setting. ( <http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=213>; accessed January 2016)

**Thursday, January 14, 2016**

**Question:**

What is the difference between level A and level D personal protective equipment (PPE) as defined by the United States Environmental Protection Agency (EPA)?

**Answer:**

**Level A protection** is required when the greatest potential for exposure to hazards exists, and when the greatest level of skin, respiratory, and eye protection is required. Examples of Level A clothing and equipment include: positive pressure, full face-piece self contained breathing apparatus (SCBA) or positive pressure supplied air respirator with escape SCBA; totally encapsulated chemical- and vapor-protective suit; inner and outer chemical-resistant gloves; and disposable protective suit, gloves, and boots.

**Level D protection** is the minimum protection required. Level D protection may be sufficient when no contaminants are present or work operations preclude splashes, immersion, or the potential for unexpected inhalation or contact with hazardous levels of chemicals. Appropriate Level D protective equipment may include: gloves; coveralls; safety glasses; face shield; and chemical-resistant, steel-toe boots or shoes. ( <http://www.epa.gov/emergency-response/personal-protective-equipment>; accessed October 2015)

**Wednesday, January 13, 2016**

**Question:**

What are the factors influencing the ocular dose of ultraviolet radiation (UVR) received by civilian aircrews during flights?

**Answer:**

The cited reference notes: "Ultraviolet radiation (UVR) increases with altitude; however, there are a number of other factors which may influence ocular exposure during flight." They go on to state: "A wide variation in ocular UVA dose was found during flights. The main factor influencing exposure was the UVR transmission of the windshield, which fell into two distinct profile types. In an aircraft with good UVA blocking properties, ocular exposure was found to be equivalent to office exposure and did not exceed international guideline limits regardless of external conditions or flight time. Most aircraft assessed had poor UVA blocking windshields, which resulted in an ocular exposure to the unprotected eye in excess of international guideline limits. No significant UVB dose was found." (Chorley AC et al. Occupational ocular UV exposure in civilian aircrew. 2016 Aerosp Med Hum Perform 87(1): 32-39)

**Tuesday, January 12, 2016**

**Question:**

Nutmeg is a spice used to flavor certain beverages and other foodstuffs. When ingested in excessive quantities a number of adverse effects have been described. What are the adverse effects associated with nutmeg ingestion? Which component of nutmeg is thought to be responsible for causing these effects? This component is actually metabolized to which sympathomimetic compound with hallucinogenic properties?

**Answer:**

The cited reference notes "When large amounts [of nutmeg] are taken, several toxic effects, including tachycardia, nausea, vomiting, agitation, and hallucinations, have been noted." The component of nutmeg believed to be responsible for causing these effects is myristicin. These authors go on to state that "Myristicin is metabolized to 3-methoxy-4,5-methylenedioxymphetamine also known as MMDA. MMDA is a sympathomimetic with hallucinogenic properties and believed to be the compound associated with nutmeg's hallucinogenic effects." (Ehrenpreis JE et al. Nutmeg poisonings: A retrospective review of 10 years experience from the Illinois Poison Center, 2001–2011. 2014 J Med Toxicol 10:148-151)

**Monday, January 11, 2016**

**Question:**

Organophosphate chemicals (herbicides and pesticides) are often used in the maintenance of golf courses. Following the application of these chemicals to a golf course what is the risk to golfers with regard to skin exposure to these chemicals?

**Answer:**

One study evaluated volunteer exposure to chlorpyrifos and carbaryl in 76 simulated rounds of golf using several measures (personal air samples, whole body dosimeters, as well as other bio- monitoring techniques). This investigation estimated exposures to golfers “following full course and full rate applications of chlorpyrifos and carbaryl were 19-68 times below current US EPA acute reference dose (RfD) values, indicating safe exposures under US EPA hazard quotient criteria.” (Putnam RA et al. Golfer exposure to chlorpyrifos and carbaryl following application to turfgrass. 2008 J Agric Food Chem 56:6616-6622)

**Friday, January 8, 2016****Question:**

Over 200 million people worldwide are afflicted with schistosomiasis (S. mansoni, S japonicum or S hematobium). Which drug provides low cost high cure rate treatment for this infection and what is the probable mechanism of action for this agent?

**Answer:**

Praziquantel is the drug of choice for schistosomiasis and provides low cost/ high cure rate treatment. The cited reference reports: “Targeting the cellular Ca2+ channels and pumps that underpin parasite Ca2+ homeostasis may realize novel antihelmintic agents. Indeed, the antischistosomal drug praziquantel (PZQ) is a key clinical agent that has been proposed to work in this manner. Heterologous expression data has implicated an action of PZQ on voltage-operated Ca2+ channels, although the relevant in vivo target of this drug has remained undefined over three decades of clinical use.” (Chan JD et al. Ca 2+ channels and praziquantel: A view from the free world. 2013 Parasitol Intl 62:619-628)

**Thursday, January 7, 2016****Question:**

The so-called “eutectic mixture of local anesthetics” (EMLA) is a mixture of 2.5 % lidocaine and 2.5% prilocaine that is used as a topically applied local anesthetic preparation. Most side effects of this preparation involve mild local skin reactions. However more severe systemic toxicity have been reported. What are the severe systemic reactions reported to be associated with the use of EMLA?

**Answer:**

The severe systemic reactions reported to be associated with the use of EMLA include methemoglobinemia, CNS toxicity, and cardiotoxicity. The cited reference notes the risk for these toxicities may be increased due to “prolonged application time, diseased skin, and concomitant use of a methemoglobin-inducing agent” as well as “excessive amounts of EMLA, large application area, previously abraded skin thermal injury induced by laser procedure, and drug-drug interactions (i.e. sertraline, oral contraceptives).” These authors also noted that application to children less than 3 months of age could pre-dispose to greater systemic absorption and concomitant systemic toxicity. (Tran AN and Koo JY. Risk of systemic toxicity with topical lidocaine/prilocaine: A review. 2014 J Drugs in Derm 13(9): 1118-1122)

**Wednesday, January 6, 2016****Question:**

What are the main psychedelic ingredients of hallucinogenic mushrooms?

**Answer:**

The main psychedelic ingredients of hallucinogenic mushrooms are psilocybin and psilocin. (Tyls F et al. Psilocybin- Summary of knowledge and new perspectives. 2014 Eur Neuropsychopharm 24:342-356)

**Tuesday, January 5, 2016****Question:**

What is the NFLIS?

**Answer:**

The DEA National Forensic Laboratory Information System (NFLIS) systematically collects results from drug chemistry analyses conducted by state and local forensic laboratories across the country. As a national drug forensic laboratory reporting system, NFLIS provides timely and detailed analytical results of drugs seized by law enforcement. It is a unique source of information for monitoring and understanding drug abuse and trafficking in the United States, including the diversion of legally manufactured drugs into illegal markets. Findings from NFLIS can also supplement existing drug data sources, including information from drug demand surveys and drug testing programs.

Over 300 state and local forensic laboratories in the United States perform nearly two million drug analyses each year. As of March 2012, 48 state laboratory systems and 91 local laboratory systems, representing 288 individual laboratories, are participating in NFLIS. In 2011, approximately 1.7 million drug analysis records were reported to NFLIS. (<http://www.deadiversion.usdoj.gov/nflis/index.html>; accessed December 2015)

**Monday, January 4, 2016****Question:**

What is the incidence of acute renal failure in patients receiving high dose methotrexate for the treatment of hematologic cancer?

**Answer:**

The cited reference notes that acute renal failure will develop in “approximately 2% of patients who receive high dose methotrexate for the treatment of hematologic cancer.” These authors further point out that “acute renal failure can occur even in the absence of toxic methotrexate levels in plasma 24 to 48 hours after infusion”. (Garneay AP et al. Acute methotrexate-induced crystal nephropathy. 2015 NEJM 373(27): 2691-2693)

**Friday, January 1, 2016****Question:**

What is favism?

**Answer:**

Per the cited reference (Schuurman 2009): “Glucose-6-phosphate dehydrogenase (G6PD) is an intra- cellular enzyme that plays a key role in the protection of erythrocytes against oxidative stress. Reduced concentrations of G6PD render erythrocytes susceptible to hemolysis under oxidative conditions induced by oxidant drugs, infection, or ingestion of fava beans. The latter is known as favism.”

These authors go on to point out “Favism is characterized by acute hemolysis, hemoglobinuria, anemia, and jaundice. Headache, nausea, back pain, chills, and fever may be present.” They further point out that “Elevated methemoglobin (metHb) levels have been observed during the hemolytic crisis of favic patients.” (Cappellini MD and Fiorelli G. Glucose-6-phosphate dehydrogenase deficiency. 2008 Lancet 371:64–74 as cited in Schuurman M et al. Severe hemolysis and methemoglobinemia following fava beans ingestion in glucose-6-phosphate dehydrogenase deficiency- case report and literature review. 2009 Eur J Pediatr 168:779-782)

**Thursday, December 31, 2015****Question:**

What are the two likely mechanisms of toxicity with regard to the inhalation of phosgene gas?

**Answer:**

The cited reference notes “Mechanistically, phosgene is postulated to cause toxicity by two different mechanisms, hydrolysis, and acylation. In the first mechanism, phosgene hydrolyses into hydrogen chloride and carbon dioxide when it comes into contact with water in the respiratory tract. At normal physiologic conditions, only small amounts of hydrochloric acid are produced. The second and likely more harmful mechanisms by which phosgene causes its effects is through acylation. By this mechanism, phosgene reacts with hydroxyl, thiol, amine, and sulphydryl groups on proteins, carbohydrates, and lipids. This mechanism causes extreme oxidative damage and quickly depletes glutathione stores, worsening the free radical damage. (Hardison LS et al. Phosgene exposure: A case of accidental industrial exposure. 2014 J Med Toxicol 10:51-56)

**Wednesday, December 30, 2015****Question:**

Male priapism is not an uncommon emergency. Female (clitoral) priapism, however, is a rare though non-emergent condition. Drug induced priapism in both sexes has been reported. Which drugs have been reported to be causative of female priapism?

**Answer:**

The cited reference notes “Common causes of priapism in men and women are medications that cause alpha-adrenergic blockade such as certain antidepressants and psychotropic medications.” These authors further note that female priapism specifically has been associated with the use of trazadone, bupropion and citalopram. (Unger CA and Walters MD. Female clitoral priapism: An over the counter option for management. 2014 J Sex Med 11:2354-2356)

**Tuesday, December 29, 2015****Question:**

Overdose with which over the counter sleep aid has been reported to be associated with potentially life threatening, delayed onset, rhabdomyolysis?

**Answer:**

Doxylamine has been reported to be associated with potentially life threatening, delayed onset, rhabdomyolysis. (Kim HJ et al. The associative factors of delayed-onset rhabdomyolysis in patients with doxylamine overdose. 2011 J Emerg Med 29(8): 903-907)

**Monday, December 28, 2015****Question:**

Which infamous disaster is widely acknowledged as the sentinel event from which the modern understanding of inhalation injury related to fires was derived?

**Answer:**

The 1942 fire at the Cocoanut Grove nightclub in Boston, Massachusetts, was the infamous disaster widely acknowledged as the sentinel event from which the modern understanding of inhalation injury related to fires was derived. There were nearly 500 fatalities and several hundred injured individuals as a result of this conflagration. The cited reference notes “[This] disaster came at a unique time in the history of burn care and resulted in a number of important advances in burn treatment, including the first comprehensive descriptions of inhalation injury....” (Saffle JR. The 1942 fire at the Cocoanut Grove nightclub. 1993 Am J Surg 166:581-591)

**Thursday, December 24, 2015****Question:**

What is a Substance Abuse Professional (SAP)?

**Answer:**

The Substance Abuse Professional (SAP) is a person who evaluates employees who have violated a DOT drug and alcohol program regulation and makes recommendations concerning education, treatment, follow-up testing, and aftercare. The following individuals are qualified to become SAPs:

Licensed physicians, licensed or certified social workers; licensed or certified psychologists; licensed or certified employee assistance professional; state-licensed or certified marriage and family therapist; or drug and alcohol counselor certified by the National Association of Alcoholism and Drug Abuse Counselors Certification Commission (NAADAC); or by the International Certification Reciprocity Consortium/Alcohol and Other Drug Abuse (ICRC); or by the National Board for Certified Counselors, Inc. and Affiliates/Master Addictions Counselor (NBCC). ( [https://www.transportation.gov/odapc/part40/40\\_281](https://www.transportation.gov/odapc/part40/40_281); accessed September 2015)

**Wednesday, December 23, 2015****Question:**

What is marijuana “wax”?

**Answer:**

Marijuana wax is a marijuana concentrate, also known as “710”, honey oil, budder, butter, butane hash oil or BHO (butane honey oil), shatter, dabs, black glass or errl. According to the cited reference: “This high potency product is made by butane extraction of plants to remove the cannabinoids followed by concentration of them by evaporating off the butane to leave a waxy residue with up to 85% THC concentration. Users refer to smoking this product as “dabbing” and it can be consumed via an electronic vapor cigarette or using an “oil rig” which is a pipe rigged for the product.” (Schneberk T et al. “A little dab will do ya”: An emergency department case series related to a new form of “high-potency” marijuana known as “wax”. 2014 Anns Emerg Med 64(4S): S139)

**Tuesday, December 22, 2015****Question:**

What is “cotton fever” and what is the clinical scenario associated with this phenomenon?

**Answer:**

The cited reference notes “cotton fever is street terminology for the post-injection fever experienced by many drug users after “shooting up” with heroin reclaimed from a previously used cotton filter.” These authors point out “Cotton fever in IVDAs is usually a benign, self-limited condition that can present in a very dramatic fashion. The onset of symptoms is thought to be from 10 to 20 min after injection. Symptoms include headache, malaise, chills and rigors, dyspnea, palpitations, nausea, emesis, abdominal pain, low back pain, myalgias, and arthralgias. Temperatures of 38.5degrees C to 40.3 degrees C develop within the first few hours after injection and patients appear acutely ill. They frequently exhibit tachycardia and tachypnea despite otherwise normal cardiorespiratory examinations and chest x-ray study. The abdomen is typically tender, with no rebound tenderness albeit voluntary guarding may be present. Diffuse muscle and joint tenderness has been noted. Laboratory investigations might reveal significant leukocytosis and transaminitis.....The syndrome is self limited and resolves spontaneously in 12-24 hours in most cases.” (Torka P and Gill S. Cotton fever: An evanescent process mimicking sepsis in an intravenous drug abuser. 2013 J Emerg Med 44(6): e385-e387)

**Monday, December 21, 2015****Question:**

On May 15, 1929, 122 people died in an infamous conflagration that has come to be known as the Cleveland Clinic Fire. How did this fire start, what burned in this famous fire and which products of combustion were likely involved?

**Answer:**

In the Cleveland Clinic Fire nitrocellulose-containing x-ray films ignited and burned producing quantities of carbon monoxide, oxides of nitrogen and arguably hydrogen cyanide, prussic acid and phosgene. Three theories as to the cause for this fire have been propounded: 1- decomposition and subsequent ignition of the nitrocellulose film was caused by a rise in temperature from uncovered steam lines in the x-ray storage area; 2- the x-ray films may have been ignited by an incandescent lamp suspended in the film area in such a way as to start decomposition of the nitrocellulose-containing film from the heat of the lamp; 3- a lighted match or cigarette was dropped on or near the x-ray films. (“Report on the Cleveland Clinic Fire, May 15, 1929” by the National Board of Fire Underwriters and the Ohio Inspection Bureau, June 4, 1929)

**Friday, December 18, 2015**

**Question:**

Direct factor Xa inhibitors (apixaban, rivaroxaban and edoxaban) are used to treat and prevent thromboembolic disease in some patients. Bleeding is a known complication associated with factor Xa inhibitors. Which agent has been designed to reverse the anticoagulant effects of factor Xa inhibitors? What is the toxicity associated with the use of this drug?

**Answer:**

According to the report of a recent study: "Andexanet reversed the anticoagulant activity of apixaban and rivaroxaban in older healthy participants within minutes after administration and for the duration of infusion without toxic effect." Additional safety and efficacy studies are being conducted. (Siegal DM et al. Andexanet alfa for the reversal of factor Xa inhibitor activity. 2015 NEJM 373:2413-2424

**Wednesday, December 16, 2015**

**Question:**

Which short-lived metabolite, when identified in urine, identifies recent heroin use?

**Answer:**

The cited reference reports "6-acetylmorphine concentrations in urine were short-live (< 7 hours) and highly variable, but were clearly associated with recent heroin exposure when present." (Cone EJ et al. Forensic drug testing for opiates. VII. Urinary excretion profile of intranasal (snorted) heroin.1996 J Analytical Tox 20:379-392)

**Tuesday, December 15, 2015**

**Question:**

What are the generally accepted causes for methamphetamine-related tooth decay also known as "meth mouth"?

**Answer:**

According to the cited reference, "the causes of methamphetamine related tooth decay may include the following: 1- The drug's acidic nature; 2- Its ability to dry the mouth reducing the amount of protective saliva around the teeth; 3-A drug induced craving of high calorie carbonated beverages; 4- The tendency of users to grind and clench their teeth; 5- The duration of the drugs effects (12 hours versus one hour for cocaine), which lead to long periods when users are not likely to clean their teeth. (Methamphetamine use and oral health. 2005 J Amer Dental Assoc 136:1491)

**Monday, December 14, 2015**

**Question:**

What is swimming induced pulmonary edema (SIPE)?

**Answer:**

According to the cited reference, SIPE is "a well known entity that affects limited members of the community. It is typically found in those who spend time in cold-water exercise with heavy swimming and surface swimming such as civilian training for Iron Man, Triathlon and military training (e.g. Navy SEALs). It tends to occur with prolonged fin use and over-hydration before the activity. Strenuous activity in cold water increase both cardiac preload and afterload. It is further theorized that a weakness or failure in the pulmonary capillaries contributes the cause of pulmonary edema [in this setting]. (Sasovetz S et al. 26 year old man with shortness of breath after open ocean swimming. 2015 Mil Med 180:1207-1208)

**Friday, December 11, 2015**

**Question:**

Ketogenic diets (KD) have been used successfully in the treatment of intractable epilepsy in pediatric patients. What is the mechanism for this modality in the treatment of epilepsy?

**Answer:**

According to the cited reference: "The mechanisms by which KD exerts its effect on seizures are expected to be complex but remain largely unknown. They possibly include enhancement of the mitochondrial respiratory

chain and ATP production. Contraindications to KD initiation are metabolic disorders, where ketones cannot be utilized such as beta oxidation defects, pyruvate carboxylase

deficiencies and porphyria. There have also been some suggestions, that mitochondrial disorders as such should be a contraindication for KD." (Sort R et al. Ketogenic diet in 3 cases of childhood refractory status epilepticus. 2013 Eur J Paediatric Neurol 17:531-536)

**Thursday, December 10, 2015**

**Question:**

What is "Flakka"?

**Answer:**

According to the cited reference "Use of a dangerous [synthetic cathinone](#) drug called alpha-pyrrolidinopentiophenone (alpha-PDP), popularly known as "Flakka," is surging in Florida and is also being reported in other parts of the country, according to news reports. Alpha-PVP is chemically similar to other synthetic cathinone drugs popularly called "bath salts," and takes the form of a white or pink, foul-smelling crystal that can be eaten, snorted, injected, or vaporized in an e-cigarette or similar device. Vaporizing, which sends the drug very quickly into the bloodstream, may make it particularly easy to overdose. Like other drugs of this type, alpha-PVP can cause a condition called "excited delirium" that involves hyperstimulation, paranoia, and hallucinations that can lead to violent aggression and self-injury. The drug has been linked to deaths by suicide as well as heart attack. It can also dangerously raise body temperature and lead to kidney damage or kidney failure." ( <http://www.drugabuse.gov/drugs-abuse/emerging-trends>; accessed, November 2015)

**Wednesday, December 9, 2015**

**Question:**

What is the primary lethal pathophysiological factor in barium poisoning, what are the significant clinical manifestations and what treatment is expected to reverse the life threatening effects of barium?

**Answer:**

According to the cited reference: "low serum potassium is the primary lethal pathophysiological factor in barium poisoning and is associated with arrhythmias, respiratory muscle paralysis and death. "Aggressive potassium administration has been shown to reverse barium toxicity." (Yu D et al. Incurable hypokalemia caused by barium chloride ingestion. 2015 Am J Med Sci 349(3): 279-281)

**Tuesday, December 8, 2015**

**Question:**

Tularemia is a zoonotic infection caused by *F. tularensis*, a gram-negative coccobacillus. *F. tularensis* has been discussed as a biological agent that might be used by terrorists. What is the drug of choice for the treatment of this infection?

**Answer:**

The cited reference notes: "Streptomycin is the historical drug of choice for the treatment of tularemia and remains a first-line agent owing to its documented efficacy, experience with its use for this infection, and approval by the Food and Drug Administration (FDA) for this indication. The FDA has approved tetracyclines as alternative agents, but they have been associated with high relapse rates in some reports. Gentamicin has also been shown to be effective, although it has not been approved by the FDA for this indication. Fluoroquinolones such as ciprofloxacin and levofloxacin are active against *F. tularensis* in vitro and have shown clinical efficacy in recent case series." (James J. et al. Back to nature. 2015 NEJM 373:2271-2276)

**Monday, December 7, 2015**

**Question:**

What ocular effects have been associated with injection of the drug known as “Krokodil”?

**Answer:**

The active component of the drug of abuse known as “krokodil” is desomorphine, an opioid analogue. According to the cited reference, “krokodil is also occasionally used concomitantly with tropicamide, a short-acting anticholinergic, resulting in mydriasis (black iris), conjunctival erythema (reddish conjunctiva), and altered mentation, contributing to the user’s overall “zombie”-like appearance.” (Shelton M. et al. Krokodil. From Russia with love. 2015 JAMA Derm 151(1): 32)

**Friday, December 4, 2015**

**Question:**

What is the HIDTA program?

**Answer:**

The HIDTA program (High Intensity Drug Trafficking Areas) is a DEA program, created by Congress with the Anti Drug Abuse Act of 1988, provides assistance to Federal, state, local, and tribal law enforcement agencies operating in areas determined to be critical drug-trafficking regions of the United States. This grant program is administered by the Office of National Drug Control Policy (ONDCP). There are currently 28 HIDTAs, which include approximately 16 percent of all counties in the United States and 60 percent of the U.S. population. ( <http://www.dea.gov/ops/hidta.shtml>; accessed November 2015)

**Thursday, December 3, 2015**

**Question:**

Acrylamide is a water-soluble, vinyl monomer that is used primarily to produce polyacrylamide polymers used in various chemical industries including water management, ore processing and molecular laboratories. While the polymer is considered to be not harmful certain exposures to the monomer may cause ataxia, skeletal muscle weakness, and weight loss. What is the characteristic neuropathological features of acrylamide neuropathy?

**Answer:**

According to the cited reference, “Distal swelling and eventual degeneration of axons in the CNS and PNS (axonopathy) have been considered to be the characteristic neuropathological features of acrylamide neuropathy.” (Lopachin RM et al. Acrylamide axonopathy revisited. 2003 Tox Appl Pharm 188:135-153)

**Wednesday, December 2, 2015**

**Question:**

What is HMX?

**Answer:**

HMX (Octogen) is an acronym for High Melting eXplosive. It is also known as octogen and cyclotetramethylene-tetranitramine. It is a colorless solid that dissolves slightly in water. Only a small amount of HMX (Octogen) will evaporate into the air; however, it can occur in air attached to suspended particles or dust. HMX (Octogen) does not occur naturally in the environment. It is made from other chemicals known as hexamine, ammonium nitrate, nitric acid, and acetic acid. HMX (Octogen) explodes violently at high temperatures. Because of this property, HMX (Octogen) is used in various kinds of explosives, rocket fuels, and burster chargers. A small amount of HMX (Octogen) is also formed in making cyclotrimethylene-trinitramine (RDX), another explosive similar in structure to HMX (Octogen). ( <http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=171>; accessed October 2015)

**Tuesday, December 1, 2015**

**Question:**

What are the dinitrocresols, what is the most commercially important dinitrocresol and what is that compound used for?

**Answer:**

Dinitrocresols are a class of manufactured chemicals that do not occur naturally in the environment. There are 18 different dinitrocresols. The most commercially important dinitrocresol, 4,6-dinitro-o-cresol (DNOC), is a yellow solid with no smell. It is used primarily for insect control and crop protection. ( <http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=218>; accessed October 2015)

**Monday, November 30, 2015**

**Question:**

What are the risks of using lidocaine with epinephrine in digital nerve blocks?

**Answer:**

A recently published literature review of this topic concluded: “Epinephrine (1:100,000-200,000) is safe to use in digital nerve blocks in healthy patients. Physiological studies show epinephrine-induced vasoconstriction to be transient. There are no reported cases of epinephrine-induced harm to patients with risk for poor peripheral circulation despite a theoretical risk of harmful epinephrine-induced vasoconstriction.” (Illicki J. Safety of epinephrine in digital nerve blocks: A literature review. 2015 J Emerg Med 49(5): 799-809)

**Friday, November 27, 2015**

**Question:**

Granulomatous pulmonary disease associated with which substance resembles pulmonary sarcoidosis?

**Answer:**

Beryllium. Beryllium may cause a granulomatous pulmonary disease known as chronic beryllium disease (CBD) which resembles pulmonary sarcoidosis. According to the cited reference, “The pathognomonic histopathologic lesion of CBD is the epithelioid granuloma, indistinguishable from those found in sarcoidosis, formed in response to a yet to be identified antigen.” (Mayer AS et al. Sarcoidosis and chronic beryllium disease: Similarities and differences. 2014 Semin Respir Crit Care Med 35:316-329)

**Thursday, November 26, 2015**

**Question:**

Arsine gas exposure may result in massive hemolysis. What is the mechanism for the development of hemolysis secondary to arsine exposure?

**Answer:**

According to the cited reference “Upon inhalation of arsine gas, it enters red blood cells and preferentially binds to hemoglobin. The arsine is oxidized to an arsenic dihydride intermediate and elemental arsenic. Both of these substances are hemolytic agents and thus contribute to red cell destruction.” (Pullen-James S et al. Occupational arsine gas exposure. 2006 J Nat Med Assoc 98(12):1998-2001)

**Wednesday, November 25, 2015**

**Question:**

What was the Harrison Narcotic Act?

**Answer:**

According to the cited reference, the Harrison Narcotic Act, enacted in 1915, required “anyone who imported, produced, sold, or dispensed “narcotics” (at that time meaning coca- as well as opium-based drugs) to register, pay a nominal tax, and keep detailed records”. The cited reference notes that through the Harrison Act “enforcement policies made it risky for [physicians] to regularly supply narcotics to addicts, giving the law its reputation as a prohibition measure”. The Harrison Act was replaced by the 1970 Controlled Substances Act. (Courtwright DT. Preventing and treating narcotic addiction-A century of federal drug control. 2015 NEJM 373:2095-2097)

**Tuesday, November 24, 2015**

**Question:**

What is the most common source for elevated carbon monoxide levels in indoor ice rinks?

**Answer:**

The most common source for potentially dangerous elevated levels of CO in indoor ice rinks has been ice re-surfacing machines that are powered by gas or propane, as opposed to electric motors. (Crewswell PD et al. Exposure to elevated carbon monoxide levels at an indoor ice arena- Wisconsin, 2014 MMWR November 20, 2015 / 64(45):1267-1270)

**Monday, November 23, 2015**

**Question:**

What is Captagon?

**Answer:**

Captagon is a “brand name “ for the drug fenethylline. It is not commercially available but rather is produced illicitly and is reportedly widely used in the Near and Middle East. The cited reference notes “Fenethylline is an N-alkylated amphetamine derivative and is metabolized to amphetamine and theophylline....”. Captagon has been recently noted in the lay press as a drug probably used by Daash terrorists for its sympathomimetic effects. (Uluçay A et al. Acute myocardial infarction associated with captagon use. 2012 Anadolı Kardiol Derg 12:181-186 and <http://timesofindia.indiatimes.com/world/middle-east/Turkey-seizes-11-million-pills-of-Syria-war-drug-reports/articleshow/49860478.cms>; accessed November 2015) [Special thanks to Tony Scalzo, MD, Dir. Div. of Med Tox at St Louis Univ School of Medicine for suggesting this topic!]

**Friday, November 20, 2015**

**Question:**

Gingival hypertrophy has been typically associated with the long-term use of phenytoin. Which other drugs have also been reported to cause gingival hypertrophy?

**Answer:**

According to the cited reference gingival hypertrophy has been associated with calcium channel blockers and cyclosporine as well as phenytoin. The mechanism responsible for the development of gingival hypertrophy associated with these drugs has not been elucidated. (Matsumura M et al. Nifedipine-induced gingival hypertrophy. 2012 Internal Med 51:121)

**Thursday, November 19, 2015**

**Question:**

What is "CAMEO"?

**Answer:**

CAMEO (Computer-Aided Management of Emergency Operations) is a system of software applications used to plan for and respond to chemical emergencies. Developed by EPA and the National Oceanic and Atmospheric Administration to assist front-line chemical emergency planners and responders, CAMEO can access, store, and evaluate information critical for developing emergency plans. ( <http://www2.epa.gov/cameo>; accessed October 2015)

**Wednesday, November 18, 2015**

**Question:**

Emtricitabine/tenofovir (Truvada) is a combination preparation containing the drugs emtricitabine and tenofovir. This combination was first approved to treat HIV-1 infection and currently is also approved as pre-exposure prophylaxis to prevent HIV-1 infection in individuals of high risk. What are the safety concerns associated with the use of this drug?

**Answer:**

According to the cited reference: “The drug must not be prescribed if the patient’s creatinine clearance is less than 60 mL per minute per 1.73 m<sup>2</sup> (1.00 mL per second per m<sup>2</sup>) because its use has been associated with renal failure and Fanconi syndrome. Although rare and not reported in premar-keting studies, lactic acidosis and severe hepatomegaly with steatosis are possible in patients at risk of liver disease, accord-ing to the drug’s manufacturer. Because both emtricitabine and tenofovir are active against hepatitis B virus, and because of the risk of rebound hepatitis following dis-continuation of therapy, this combination should be used with caution in patients coinfectd with hepatitis B virus.” (Coutinho B and Prasad R. Emtricitabine/tenofovir (Truvada) for HIV prophylaxis. 2013 Am Fam Physician 88(8):535-540)

**Tuesday, November 17, 2015**

**Question:**

Ivabradine is a novel anti-anginal agent that has been reported to be associated with phosphenes. What are phosphenes?

**Answer:**

The cited reference notes: “The visual sensations evoked by stimuli other than luminance changes are known as phosphenes. Phosphenes can be spontaneous or provoked in a number of ways including a gentle pressure on the eyelids...” Ivabradine has been reported to cause phosphene-like phenomena. (Cervetto L et al. Cellular mechanisms underlying the pharmacological induction of phosphenes. 2007 Br J Pharm 150:383-390)

**Monday, November 16, 2015**

**Question:**

What is the difference between “summer hypersensitive pneumonitis” and so-called “hot tub lung”?

**Answer:**

According to the cited reference “Summer-type hypersensitivity pneumonitis (HP) is caused by the inhalation of *Trichosporon asahii* or *mucoïdes* during the hot and humid summer season, while hot tub lung is a diffuse granulomatous lung disease that results from the inhalation of water aerosols containing non-tuberculous mycobacteria.” (Minomo S. et al. A unique case of hot tub lung worsening during the winter. 2015 Internal Med 54:491-495)

**Friday, November 13, 2015**

**Question:**

What characterizes food poisoning related to the ingestion of *Bacillus cereus* and which foods are usually involved in the development of *B. cereus*-related gastrointestinal illness.



**Answer:**

According to the cited reference “Food poisoning by *B. cereus* can either be caused by an infection or an intoxication, which leads to a diarrheal or an emetic type of illness, respectively. Foods often related to diarrheal food poisoning include meat products, soups, vegetables, sauces and dairy products, while those related to the emetic type of syndrome are mainly rice and pasta” (McIntyre, L., et al. Identification of *Bacillus cereus* group species associated with food poisoning outbreaks in British Columbia, Canada. Appl. Environ. Microbiol. 2008, 74, 7451–7453. As cited in Senesi S and Ghelardi E. Production, secretion and biological activity of *Bacillus cereus* enterotoxins. 2010 Toxins 2:1690-1703)

**Thursday, November 12, 2015****Question:**

What are “Beau lines” and exposure to which medications may cause the development of this abnormality?

**Answer:**

According to the cited reference, Beau lines are fine, transverse, depressed, evenly spaced, parallel lines that develop in human nails. These changes are related to “interruption of mitotic activity of the proximal nail matrix” in patients receiving chemotherapy with such drugs as daunorubicin, cytarabine, docetaxel. Beau lines may occur in as many as 44% of patients receiving taxanes (drugs derived from plants of the genus *taxus*). Beau lines may also develop in patients suffering a variety of systemic illness. (Huang T and Chao T. Mees lines and Beau lines after chemotherapy. 2010 CMAJ 182(3): E149)

**Wednesday, November 11, 2015****Question:**

What is areca nut and what adverse health problems have been associated with its use?

**Answer:**

The cited reference notes “Areca nut is the fruit of the Areca catechu tree that contains alkaloids (particularly arecoline) and tannins, which are the nut’s most active ingredients. In most of the world, the nut is habitually chewed with other ingredients (e.g. leaf from Piper betle, slaked lime, tobacco and spices). When the nut is chewed with other ingredients, generally betel leaf, lime, with or without tobacco, it is called a betel quid. Approximately 10-20% of the world’s population chews areca (betel) nut. The alkaloids and nitrosamines in areca nut are considered carcinogens, and could produce precancerous lesions or conditions – now referred to as potentially malignant disorders – that are likely to develop into oral cancer.” (Paulino YC et al. Screening for oral potentially malignant disorders among areca (betel) nut chewers in Guam and Saipan. 2014 BMC Oral Health 14:151-159)

**Tuesday, November 10, 2015****Question:**

The antimalarial drugs chloroquine and hydroxychloroquine are associated with the development of serious ocular toxicity. What is the risk for fetal ocular toxicity when pregnant women are treated with these drugs?

**Answer:**

The cited reference reports “Current evidence suggests no fetal ocular toxicity of antimalarial medications during pregnancy. The clinical significance of early electroretinogram anomalies reported in a small subset of infants remains to be established. Larger follow up studies are warranted to confirm low risk of ocular toxicity in children following antenatal exposure to antimalarial medications.” (Osadchy A et al. Ocular toxicity in children exposed *in utero* to antimalarial drugs: Review of the literature. 2011 J Rheumatol 38:2504-2508)

**Monday, November 9, 2015****Question:**

N-hexane is an organic solvent that is frequently used in a variety of industries including printing, food processing, and electronics. High dose, long-term exposure to this chemical can result in the development of peripheral polyneuropathy. What is the metabolite of n-hexane that is responsible for the development of this neuropathy?

**Answer:**

2,5 hexanedione is the metabolite of n-hexane responsible for the development of the peripheral neuropathy associated with occupational n-hexane exposure. (Wang C et al. Electrophysiological follow-up of patients with chronic peripheral neuropathy induced by occupational intoxication with n-hexane. 2014 Cell Biochem Biophys 70:579-585)

**Friday, November 6, 2015****Question:**

Treating maternal cancer during pregnancy exposes the developing fetus to potentially dangerous chemotherapeutic drugs. What is the effect of prenatal exposure to maternal cancer with or without treatment with regard to cognitive, cardiac, or general development of children in early childhood?

**Answer:**

A recently reported study involving 129 children whose mothers had cancer reported “Prenatal exposure to maternal cancer with or without treatment did not impair the cognitive, cardiac, or general development of children in early childhood. Prematurity was correlated with a worse cognitive outcome, but this effect was independent of cancer treatment.” (Armant F et al. Pediatric outcome after maternal cancer diagnosed during pregnancy. 2015 NEJM, 373:1824-1834)

**Thursday, November 5, 2015****Question:**

Which beta-blocking agent has been noted to cause false positive urine screening for amphetamines?

**Answer:**

Labetalol has been noted to cause false positive urine screening for amphetamines. (Moeller KE et al. Urine drug screening: Practical guide for clinicians. 2008 Mayo Clin Proc 83(1): 66-76)

**Wednesday, November 4, 2015****Question:**

So-called “drumstick fingers” and “watch glass nails” have been associated with unprotected and prolonged occupational exposure to which chemical?

**Answer:**

Vinyl chloride has classically been associated with acro-osteolysis however “drumstick fingers” and “watch glass nails” have been associated with late stages of occupationally based vinyl chloride related disease. (Gama C et al. Occupational acro-osteolysis. 1978 J Bone Joint Surgery 60(1): 86-90) [see the cited article for a fantastic photo of “drumstick fingers” and “watch glass nails” ]

**Tuesday, November 3, 2015****Question:**

What is the half-life and time to steady state for digoxin?

**Answer:**

According to the cited reference “The half-life and time to steady-state varies by patient and is dependent on the renal function. In patients with normal renal function, the half-life ranges from 1.5 to 2 days. This is prolonged anywhere from 3.5 to 5 days in patients with moderate to severe renal dysfunction. Patients with normal renal function reach steady state in 5 to 7 days after initiation of therapy, whereas it may take up to 15 to 20 days in patients with impaired renal function.” (Ehle M et al. Digoxin: Clinical Highlights: A review of digoxin and its use in contemporary medicine. 2011 Crit Pathways in Cardiol 10:93-98)

**Monday, November 2, 2015**

**Question:**

5-fluorouracil (5-FU) is an important agent in the treatment of a variety of cancers. Cardiotoxicity is a prime concern with the systemic administration of this anti neoplastic drug. What are the most severe adverse cardiac effects associated with the use of 5-FU?

**Answer:**

According to the cited reference, the most severe cardiac complications of 5-FU are heart failure, cardiac arrhythmias and myocardial ischemia. (Lamberti M et al. A mechanistic study on the cardiotoxicity of 5-fluorouracil in vitro and clinical and occupational perspectives. 2014 Tox Letters 227:151-156)

**Friday, October 30, 2015**

**Question:**

What is the leading cause of injury death in the US?

**Answer:**

According to the cited reference "Drug overdose is the leading cause of injury death in the United States. The death rate from drug overdose in the United States more than doubled during 1999–2013, from 6.0 per 100,000 population in 1999 to 13.8 in 2013. The increase in drug overdoses is attributable primarily to the misuse and abuse of prescription drugs, especially opioid analgesics, sedatives/tranquilizers, and stimulants." (Paulozzi LJ et al. Controlled Substance Prescribing Patterns — Prescription Behavior Surveillance System, Eight States, 2013. MMWR October 16, 2015 / 64(SS09):1-14)

**Thursday, October 29, 2015**

**Question:**

What is the half-life of carboxyhemoglobin in persons treated with 100% oxygen at atmospheric pressure?

**Answer:**

One study of 93 carbon monoxide poisoned patients treated with 100% oxygen at atmospheric pressure reported the half-life of carboxyhemoglobin to be 74 +/- 25 minutes. These authors point out that some reports indicate the half-life of carboxyhemoglobin in patients treated with 100% oxygen to be as long as 130 +/- 130 minutes. In contrast, a frequently quoted average for the half-life of carboxyhemoglobin is 80 minutes in persons treated with 100% oxygen however this was based on a study of only two volunteers. (Weaver LK et al. Carboxyhemoglobin half-life in carbon monoxide poisoned patients treated with 100% oxygen at atmospheric pressure. 2000 Chest 117(3): 801-808)

**Wednesday, October 28, 2015**

**Question:**

Which anesthetic gas is used as a recreational drug and may cause megaloblastic anemia by blocking the conversion of vitamin B12 from the reduced to the oxidized form?

**Answer:**

The cited reference notes that "Nitrous oxide [is] an anesthetic gas that has become increasingly popular for use as a recreational drug, [and] may cause megaloblastic anemia by blocking the conversion of vitamin B 12 from the reduced to the oxidized form".(Hesdorffer CS and Longo DL. Drug-induced megaloblastic anemia. 2015 NEJM 373:1649-1658)

**Tuesday, October 27, 2015**

**Question:**

What is the prevalence of nickel allergy and what are the most common sources for nickel induced allergy?

**Answer:**

According to the cited reference nickel allergy affects 10-30% of women and 1-3% of men. The primary causes for nickel exposure leading to the development of allergy involves prolonged exposure to nickel-releasing items including jewelry, buttons, zippers and belts. (Thyssen JP et al. The epidemiology of contact allergy in the general population-prevalence and main findings. 2007 Contact Dermatitis 57:287-299)

**Monday, October 26, 2015**

**Question:**

What is the prevalence of nickel allergy and what are the most common sources for nickel causing allergy?

**Answer:**

According to the cited reference nickel allergy affects 10-30% of women and 1-3% of men. The primary causes for nickel exposure leading to the development of allergy involves prolonged exposure to nickel-releasing items including jewelry, buttons, zippers and belts. (Thyssen JP et al. The epidemiology of contact allergy in the general population-prevalence and main findings. 2007 Contact Dermatitis 57:287-299)

**Friday, October 23, 2015**

**Question:**

What are the most common triggers for anaphylaxis in infants?

**Answer:**

According to the cited reference "Anaphylaxis in infants can be triggered by a variety of agents, of which foods are by far the most common. Typical culprits are cow's milk, egg, and peanut, but any food can be implicated, including tree nuts, soy and other legumes, fish, vegetables, fruits, and grains, such as wheat and rice. Food-induced anaphylaxis can occur after direct ingestion or indirect ingestion through breast milk; rarely, it is triggered by skin contact with food or vomitus, or inhalation of vapors from cooking food." (Simons FES and Sampson HA. Anaphylaxis: Unique aspects of clinical diagnosis and management in infants (birth to age 2 years). 2015 J Allergy Clin Immunol 135(5):

**Thursday, October 22, 2015**

**Question:**

Methylene chloride (also known as dichloromethane) is well known to be metabolized to carbon monoxide in mammals. Consequently human exposure may result in the development of carbon monoxide toxicity. Which products and processes might be expected to contain or include methylene chloride?

**Answer:**

According to the cited reference "Methylene chloride is used as a solvent in paint strippers and removers (30 %), in adhesives (20 %), as a propellant in aerosols (10 %), as a solvent in the manufacture of pharmaceuticals and drugs (10 %), in chemical processing (10 %), as a metal cleaning and finishing solvent (10 %), and in urethane foam blowing (5 %). Other uses make up the remaining 5 %. Methylene chloride is also widely used in applications such as metal cleaning and degreasing, polyurethane foam manufacturing, triacetate film and fiber manufacturing, food extraction, and aerosol propellants. Current household products that may contain methylene chloride include lubricants, valve cleaners, and degreasers for automobiles, adhesive and varnish removers, paint strippers, and one household herbicide. Methylene chloride is present in these products at percentages ranging from 1 to 90 %." (Liu T et al. Occupational exposure to methylene chloride and risk of cancer: a meta-analysis. 2013 Cancer Causes Control 24: 2037-2049)

**Wednesday, October 21, 2015**

**Question:**

Anabolic steroids are used by athletes of all ages as well as other individuals. These drugs are associated with a variety of adverse effects including certain feminizing effects such as gynecomastia in males. Which drug is often used to oppose the feminizing effects of anabolic steroids?

**Answer:**

Tamoxifen is often used to oppose the feminizing effects of anabolic steroids. (Talih F et al. Anabolic steroid abuse: Psychiatric and physical costs. 2007 Clev Clinic J Med 74(5): 341-352)

**Tuesday, October 20, 2015****Question:**

What are the clinical characteristics associated with so-called toluene related encephalopathy?

**Answer:**

According to the cited reference “toluene encephalopathy is described by cognitive dysfunction (especially prefrontal), cerebellar dysfunction, spasticity, dementia, seizures, coma and/or radiographic changes termed leukoencephalopathy”. (Tormoehlen LM et al. Hydrocarbon toxicity: A review. 2014 Clin Tox 52:479-489)

**Monday, October 19, 2015****Question:**

What is the interval between consuming certain fish and symptom onset with regard to ciguatera fish poisoning?

**Answer:**

One recent report of six cases of ciguatera fish poisoning described the interval between consuming fish and symptom onset. This report stated the interval ranged from 3 to 7.25 hours with a median interval of 3 hours. (Use of Surveillance Systems in Detection of a Ciguatera Fish Poisoning Outbreak — Orange County, Florida, 2014. October 16, 2015 MMWR 64(40); 1142-1144)

**Friday, October 16, 2015****Question:**

Occupational exposure to silica has been linked to the development of which rheumatologic conditions?

**Answer:**

Occupational exposure to silica has been linked to the development of rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis and dermatomyositis. (Blanc PD et al. Prospective risk of rheumatologic disease associated with occupational exposure in a cohort of male construction workers. 2015 Am J Med 128(10): 1094-1101.

**Thursday, October 15, 2015****Question:**

What is the most powerful natural nicotinic agonist ever identified?

**Answer:**

According to the cited reference, “One of the greatest discoveries over the past 15 years has been the isolation of epibatidine from the skin of Ecuadorian poison frog, *Epipedobates tricolor*.” These authors note: “Epibatidine is the most powerful natural nicotinic agonist known”. (Philippe G and Angenot L. Recent developmngnet in the field of arrow and dart poisons. 2005 J Ethnopharm 100:85-91)

**Wednesday, October 14, 2015****Question:**

Both oral and injectable extended release forms of naltrexone are used to treat chronic alcoholism. What safety issue should be considered when choosing oral naltrexone versus injectable extended release naltrexone?

**Answer:**

Oral naltrexone has been associated with the development of hepatotoxicity. The cited study of 624 patients randomly assigned to injectable extended release naloxone treatment versus placebo concluded “extended release formulation of naltrexone does not appear to be hepatotoxic when taken at the recommended clinical doses in actively drinking alcohol dependent patients.” (Lucey MR et al. Hepatic safety of once-monthly injectable extended release naltrexone administered to actively drinking alcoholics. 2008 Alc Clin Exp Res 32(3): 498-504)

**Tuesday, October 13, 2015****Question:**

Buprenorphine is a semisynthetic opioid, derived from thebaine, which acts as a partial mu receptor agonist and a kappa receptor antagonist. This drug is often used in the treatment of opiate dependent individuals. Which drug, in combination with buprenorphine, has been responsible for the majority of fatal drug-drug interactions involving buprenorphine?

**Answer:**

The cited reference notes that “fatalities involving buprenorphine alone seem very unusual: in this series all cases but one involved a concomitant intake of psychotropics.” These authors report that with regard to buprenorphine deaths “Benzodiazepines ranked first in association” and they suggest that when used with buprenorphine, “the CNS-depressant effects of buprenorphine may be synergically potentialized by some benzodiazepines (otherwise almost harmless if taken alone).” (Kintz P. Deaths involving buprenorphine: a compendium of French cases. 2001 For Sci Int 121: 65-69)

**Monday, October 12, 2015****Question:**

What is the concept of “adverse selection” with regard to the prescribing of long-term opioid therapy for chronic pain?

**Answer:**

The cited reference describes “adverse selection” as “a process where the likelihood of a patient receiving an opioid regimen increases as the associated risks increase. For example, a history of depression or other common mental health disorders increases the likelihood of receiving long term opioid therapy (LtOT) by 3- to 4-fold, a history of alcohol or non-opioid drug abuse increases the likelihood by 4–5 times, and a history of opioid abuse or dependence makes LtOT 5–10 times more likely. Furthermore, these high-risk patients with substance abuse and mental health disorders are more likely to receive high-risk opioid regimens involving high-opioid daily doses, high-potency DEA Schedule II opioids (opioids with medical use but high risk for abuse), and concurrent sedative-hypnotic medications.” (Saunders KW, et al. Concurrent use of alcohol and sedatives among persons prescribed chronic opioid therapy: prevalence and risk factors. 2012 J Pain;13:266–75 as cited in Sullivan MD and Howe CQ. Opioid therapy for chronic pain in the United States: Promises and perils. 2013 Pain 154; S94-S100)

**Friday, October 9, 2015**

**Question:**

Several drugs are currently considered somewhat effective in the treatment of alcohol abuse disorders (AUDs). The most commonly prescribed medications for AUDs are naltrexone and acamprosate. The anti-epileptic drug topiramate has also been proposed as a treatment for AUDs. What is the purported clinical effect and mechanism of action for topiramate when used to treat AUDs?

**Answer:**

According to the cited meta-analysis, "Topiramate is hypothesized to "decrease alcohol reinforcement and the propensity to drink" by reducing craving for alcohol through antagonizing the glutamate receptors and inhibiting dopamine release". (Blodgett JC et al. A meta-analysis of topiramate's effects for individuals with alcohol use disorders. 2014 Alcoholism: Clin Exp Res 38(6): 1481-1488)

**Thursday, October 8, 2015**

**Question:**

Stingray stings are not uncommon occurrences along the U.S. coast. These stings can result in severe pain and other untoward symptoms. Various proteins as well as serotonergic and cholinergic chemicals are known to be components of the venom however the precise venom constituent responsible for the severe symptoms has not been elucidated. What is the most commonly recommended treatment for the severe venom related pain due to stingray stings?

**Answer:**

According to the cited reference "The most commonly prescribed treatment of stingray injuries is irrigation with saline or fresh water followed by immersion of the stung extremity in hot water at a temperature of 43.3° to 46.1°C (110° to 115°F). Hot water is thought to accelerate the denaturing of the heat-labile toxin, although the optimal range of temperature needed for this process is not known. " These authors go on to state "In our series, hot water immersion alone was effective in eliminating the pain associated with most stingray envenomations. This confirms a previous report that suggested that hot water therapy was successful as a first- line analgesic in 9 of 10 patients. There were no burns or other complications from hot water immersion in our cases." (Clark RF et al. Stingray envenomation: A retrospective review of clinical presentation and treatment in 119 cases. 2007 J Emerg Med 33(1): 33-37)

**Wednesday, October 7, 2015**

**Question:**

What are the most common EKG changes associated with beta-blocker toxicity?

**Answer:**

According to the cited reference "Most commonly, negative dromotropic effects will be appreciated, such as first-degree AV block and intraventricular conduction delays. A negative chronotropic effect, as demonstrated by a heart rate of less than 60 beats/min, appears to be a less common manifestation." (Love JN et al. Electrocardiographic changes associated with beta-blocker toxicity. 2002 Anns Emerg Med 40(6): 603-610)

**Tuesday, October 6, 2015**

**Question:**

What is the "MOTHER project"?

**Answer:**

The MOTHER project (Maternal Opioid Treatment: Human Experimental Research project) is a multi-center, randomized, double-blind, double-dummy, flexible-dosing, parallel-group clinical trial examining the comparative safety and efficacy of methadone and buprenorphine for the treatment of opioid dependence in pregnant women and their neonates. One of the conclusions of the MOTHER project as published in the cited reference is that the "results are consistent with the use of buprenorphine as an acceptable treatment for opioid dependence in pregnant women." (Jones HE, et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. 2010 NEJM 363:2320-2331)

**Monday, October 5, 2015**

**Question:**

Recently promulgated guidelines have encouraged the use of breast milk for infants at risk for developing the opioid-related neonatal abstinence syndrome. What is the rationale for this recommendation?

**Answer:**

Guidelines issued by the American College of Obstetricians and Gynecologists, the American Academy of Pediatrics, and the Academy of Breast Feeding Medicine have "encouraged the selective use of breast milk in some infants because of growing evidence that breast milk can reduce infants' symptoms and minimize pharmacologic treatment, outweighing the harm of some drug transmission, which is typically minimal when mothers are in treatment programs." (Tolia VN et al. Increasing incidence of the neonatal abstinence syndrome in U.S Neonatal ICUs. 2015 NEJM 372:2118-2125)

**Friday, October 2, 2015**

**Question:**

What are the predominantly used precursors for the illicit manufacture of 3,4 methylenedioxymethamphetamine (MDMA)?

**Answer:**

According to the cited reference, "Safrole, the main compound in the essential oil of several plants of the Laurel family (Lauraceae), and its secondary product piperonylmethylketone are the predominantly used precursors for the illicit synthesis of 3,4-methylenedioxymethamphetamine (MDMA) which is, in turn, the most common active ingredient in Ecstasy tablets." (Schaffer M et al. Forensic profiling of sassafras oils based on comprehensive two-dimensional gas chromatography. 2013 For Sci International 229:108-115)

**Thursday, October 1, 2015**

**Question:**

What drug has been called "reverse marijuana"?

**Answer:**

Rimonabant is a selective CB1 receptor antagonist, sometimes known as "reverse marijuana", has been shown to have anorexic effects (while cannabis is known to increase appetite) and has been widely investigated as a treatment for obesity. This drug was withdrawn from the US market in 2008 due to possible severe psychiatric adverse effects. However, as stated by the cited reference, rimonabant and the endocannabinoid system is "currently a top contender as a therapeutic target for the treatment of obesity". (Pataký Z et al. Efficacy of rimonabant in obese patients with binge eating disorder. 2013 Exp Clin Endocrinol Diabetes 121(01): 20-26)

**Wednesday, September 30, 2015**

**Question:**

What is the potential utility of the Chinese herbal root known as kudzu?

**Answer:**

Kudzu is a derivative of the plant Pueraria lobata that contains high concentrations of isoflavones. The cited reference notes: "Although the mechanism of action remains unclear it is widely accepted that the isoflavones found in kudzu are effective in reducing alcohol intake in a number of nonhuman mammalian models." The cited reference reports their study population demonstrated "significant reduction in the number of beers consumed that was paralleled by an increase in the number of sips and the time to consume each beer and a decrease in the volume of each sip" but without an effect in the urge to drink alcohol. (Lukas SE et al. An extract of the Chinese herbal root kudzu reduces alcohol drinking by heavy drinkers in a naturalistic setting. 2005 Alcohol Clin Exp Res 29(5): 756-762)

**Tuesday, September 29, 2015**

**Question:**

Is methamphetamine legally available in the United States today?

**Answer:**

Yes, methamphetamine hydrochloride is legally available in the United States in the form of the drug known as Desoxyn, classified as a class II, indicated for the treatment of attention-deficit hyperactivity disorder (ADHD). ( <http://www.fda.gov/downloads/drugs/drugsafety/ucm088582.pdf>, accessed September 2015)

**Monday, September 28, 2015**

**Question:**

Is methamphetamine legally available in the United States today?

**Answer:**

Yes, methamphetamine hydrochloride is legally available in the United States in the form of the drug known as Desoxyn. This drug is classified as DEA class II and is indicated for the treatment of attention-deficit hyperactivity disorder (ADHD). ( <http://www.fda.gov/downloads/drugs/drugsafety/ucm088582.pdf>, accessed September 2015)

**Friday, September 25, 2015**

**Question:**

What was the Fernald Medical Monitoring Program?

**Answer:**

According to the cited reference, "the Fernald Medical Monitoring Program (FMMP) provided health screening and promotion services to 9775 persons who resided within close proximity to the Feed Material Production Center (FMPC), a former uranium processing plant at Fernald, Ohio. The FMMP was a result of a class action lawsuit against National Lead of Ohio (NLO) and the U.S. Department of Energy (DOE) on behalf of persons who lived near the plant and was the largest medical monitoring program created through class action litigation as a response to an environmental exposure." (Wones R. et al. Medical monitoring: A beneficial remedy for residents living near an environmental hazard site. 2009 J Occup Environ Med 51:1374-1383)

**Thursday, September 24, 2015**

**Question:**

Boric acid is a component of some insecticides but the ingestion of this substance is not a common problem. The signs and symptoms associated with boric acid ingestion are relatively non-specific and usually include nausea, vomiting and diarrhea. What are the characteristic skin manifestations associated with boric acid ingestion?

**Answer:**

According to the cited reference "Skin changes follow within hours of ingestion, and are characterized by a diffuse, intensely erythematous, 'boiled lobster' appearing rash, localized at first to the axillary and inguinal areas before becoming generalized. These changes may involve the palms and soles, and mucous membranes, shortly after the erythematous stage extensive desquamation occurs. The degree to which the skin manifestations accompany intoxication is variable, and in fact some cases lack any skin changes at all. Alopecia totalis has also been reported, as have vesiculo-pustular lesions." These authors also point out that boric acid ingestion may be associated with feces and vomitus with "a peculiar blue-green hue". (Webb DV et al. Boric acid ingestion clinically mimicking toxic epidermal necrolysis. 2013 J Cutan Path 40: 962-965)

**Wednesday, September 23, 2015**

**Question:**

What are "biopesticides"?

**Answer:**

According to the EPA, "[Biopesticides](http://www.epa.gov/pesticides/about/types.htm) are certain types of pesticides derived from such natural materials as animals, plants, bacteria, and certain minerals. For example, canola oil and baking soda have pesticidal applications and are considered biopesticides. Biopesticides fall into three major classes: 1- Microbial pesticides, 2- Plant Incorporated Protectants (PIPs) and 3- Biochemical pesticides. Biochemical pesticides are naturally occurring substances that control pests by non-toxic mechanisms. Conventional pesticides, by contrast, are generally synthetic materials that directly kill or inactivate the pest. Biochemical pesticides include substances, such as insect sex pheromones, that interfere with mating, as well as various scented plant extracts that attract insect pests to traps. ( <http://www.epa.gov/pesticides/about/types.htm>, accessed September 2015)

**Tuesday, September 22, 2015**

**Question:**

Oral naltrexone is often recommended for the treatment of alcohol use disorders. What are the contraindications for the use of oral naltrexone in treating these problems?

**Answer:**

According to the cited reference "Oral naltrexone is contraindicated for patients with acute hepatitis or liver failure (and has precautions for other hepatic disease) and for those currently using opioids or with anticipated need for opioids, and it can precipitate severe withdrawal for patient dependent on opioids." Interestingly the prescribing information for injectable naltrexone does not include contraindications for patients with acute hepatitis or liver failure. ("Pharmacotherapy for Adults with Alcohol-Use Disorders in Outpatient Settings: A monograph". 2015 Agency for Healthcare Research and Quality. [www.ahrq.gov](http://www.ahrq.gov), accessed September 2015)

**Monday, September 21, 2015**

**Question:**

With regard to alcohol withdrawal, what is the phenomenon known as "kindling"?

**Answer:**

According to the cited reference, "Kindling" is "a term defined as a change in brain physiology caused by repeated sub-threshold levels of electrical stimulation until epileptiform activity results in seizure activity to a subthreshold stimulus. Importantly, this cumulative kindling process that increases the sensitivity to stimulus-induced seizure activity is relatively permanent." (Breese GA et al. Chronic alcohol neuroadaptation and stress contribute to susceptibility for alcohol craving and relapse. 2011 Pharmacology & Therapeutics 129:149-171)

**Friday, September 18, 2015**

**Question:**

What is the "Cancer Slope Factor"?

**Answer:**

The United States Environmental Protection Agency (EPA) defines "Cancer Slope Factor" as "An upper bound, approximating a 95% confidence limit, on the increased cancer risk from a lifetime exposure to an agent. This estimate, usually expressed in units of proportion (of a population) affected per mg/kg/day, is generally reserved for use in the low-dose region of the dose-response relationship, that is, for exposures corresponding to risks less than 1 in 100." ( [click here](#), Accessed September 2015)

**Thursday, September 17, 2015**

**Question:**

What is the spectrum of clinical problems manifested by those who present to hospital emergency departments under the influence of K2?

**Answer:**

According to the cited reference, “K2 users present to emergency departments with severe adverse effects including hypertension, visual and auditory hallucinations, tachycardia, sinus bradycardia, chest pain, dysrhythmias, seizures, psychosis, intracranial hemorrhage, and even death. (Chimalakonda KC et al. Cytochrome P450-mediated oxidative metabolism of abused synthetic cannabinoids found in K2/spice: Identification of novel cannabinoid receptor ligands. 2012 Drug Met and Disposition 40(11):2174-2184)

**Wednesday, September 16, 2015****Question:**

What is the so-called fetal solvent syndrome?

**Answer:**

This term has often been applied to prenatal exposure to toluene via inhalant abuse by pregnant individuals. According to the cited reference, “The term “fetal solvent syndrome” has been adopted to describe a constellation of morphological and behavioral effects following the model of fetal alcohol syndrome and comparing the phenotype of toluene embryopathy to the effects of prenatal alcohol exposure.” “In particular, cranio-facial features, linked with the abuse of either toluene or alcohol include small palpebral fissures, a thin upper lip and midface hypoplasia.” “.....more consistently after prenatal toluene than in fetal alcohol syndrome, included micrognathia, ear abnormalities, a narrow bifrontal diameter, abnormal scalp hair patterning, a down-turned corners of the mouth and a large fontanelle.” (Bowen SE and Hannigan JH. Developmental toxicity of prenatal exposure to toluene. 2006 AAPS Journal 8(2): E419-E424)

**Tuesday, September 15, 2015****Question:**

What is ayahuasca?

**Answer:**

According to the cited reference, “Ayahuasca is an Amazonian psychotropic plant tea combining the 5-HT<sub>2A</sub> agonist N,N-dimethyltryptamine (DMT) and monoamine oxidase-inhibiting beta-carboline alkaloids that render DMT orally active. The tea, obtained from Banisteriopsis caapi and Psychotria viridis, has traditionally been used for religious, ritual and medicinal purposes by the indigenous peoples of the region. More recently the syncretistic religious use of ayahuasca has expanded to the United States and Europe.” (dos Santos RG et al. Autonomic, neuroendocrine and immunological effects of ayahuasca. A comparative study with D- amphetamine. 2011 J Clin Psychopharm 31:717-726)

**Monday, September 14, 2015****Question:**

What are Biot’s respirations and with what group of drugs is this breathing pattern associated?

**Answer:**

Individuals taking opioids on a chronic basis may develop sleep disordered breathing including central apnea and ataxic and irregular breathing patterns sometimes known as Biot’s respirations. In these cases CPAP is usually unsuccessful as therapy and in many of these cases CPAP has been reported to actually worsen apnea. (Farney RJ et al. Adaptive servoventilation (ASV) in patients with sleep disordered breathing associated with chronic opioid medications for non-malignant pain. 2008 J Clin Sleep Med 4(4): 311-319)

**Friday, September 11, 2015****Question:**

Cannabidiol is a non-psychoactive endogenous cannabinoid that has been proposed as a potentially effective anti-seizure compound. What is the proposed mechanism for this anti-seizure effect?

**Answer:**

Cannabidiol is the propyl variant of the cannabinoid, cannabidiol. A recent review article has emphasized the anti-seizure effects of this cannabinoid. The cited reference notes “Like cannabidiol, cannabidiol has anti-seizure effects that are independent of the endocannabinoid system and may function by means of its influence on TRP (transient receptor potential) channels or by lowering 2-AG (2-arachidonoylglycerol) synthesis through the inhibition of DAGL- $\alpha$  (diacylglycerol lipase alpha).” (Friedman D. and Devinsky O. Cannabinoids in the treatment of epilepsy. 2015 NEJM 373:1048-1058)

**Thursday, September 10, 2015****Question:**

As a consequence of the epidemic of opioid abuse in the US, some drug manufacturers have sought to develop “abuse-deterrent” opioid products. What are the FDA requirements regarding “claims of abuse deterrence” in labeling of such opioid formulations?

**Answer:**

According to the cited reference “the FDA requires that laboratory tests first be performed to assess how easily the abuse-deterrent properties of the formulation can be compromised. In vivo studies should then compare the pharmacokinetic profiles of the formulation before and after manipulation. Based on these results, a randomized, double blind, placebo- and active controlled study should evaluate subjective effects of the formulation, such as differences in “drug liking” in recreational drug users.” (The Medical Letter August 31, 2015. 57(1476): 119-121)

**Wednesday, September 9, 2015****Question:**

Amyloidosis (amyloid A amyloidosis) with renal involvement has been reported to occur in some drug addicts. With what process has amyloidosis in addicts been linked?

**Answer:**

Amyloidosis has been reported in some addicts who engage in “skin popping” (subcutaneous injection) with concomitant development of chronic skin infections. (Bakir AA and Dunea G. Drugs of abuse and renal disease. 1996 Curr Opin in Nephrol and Hypertension 5:122-126)

**Tuesday, September 8, 2015****Question:**

What are the so-called “BTEX” compounds?

**Answer:**

“BTEX” is an abbreviation that stands for the volatile organic compounds: “benzene, toluene, ethylbenzene and xylenes”. (Moolla R et al. Occupational exposure of diesel station workers to BTEX compounds at a bus depot. 2015 Int J Environ Res Public Health 12(4): 4101-4115)

**Monday, September 7, 2015****Question:**

What is the so-called “shake and bake” method of methamphetamine production and how does this process create a hazard for the meth-maker?

**Answer:**

The “shake and bake” methamphetamine making process became popular in the late 1980’s after restrictions on retail sales of common precursor chemicals (ephedrine and pseudoephedrine) were enacted. According to the cited reference, “this method involves shaking smaller amounts of precursor chemicals in a 2 liter plastic bottle, which frequently bursts, causing burns and environmental contamination”. (Meinkova N. Injuries from methamphetamine related chemical incidents- Five states, 2001-2012. MMWR August 28, 2015, 64(33):909-912)

**Friday, September 4, 2015****Question:**

In 2008, 23 intravenous methcathinone users in Latvia were reported as having developed manganese related Parkinsonism with significant changes in the basal ganglia as documented on brain MRI. What was the purported etiology of the manganese in these cases?

**Answer:**

According to the cited reference “The methcathinone (in the referenced cases) was manufactured under home conditions by potassium permanganate oxidation of ephedrine or pseudoephedrine”. In the cases discussed elevated levels of manganese were documented as well. (Stepens A et al. A Parkinsonian syndrome in methcathinone users and the role of manganese. 2008 NEJM 358:1009-1017)

**Thursday, September 3, 2015****Question:**

Alcohol use by drivers is well recognized as a risk factor for motor vehicle crashes. What is the role of alcohol in pedestrians who are struck by motor vehicles?

**Answer:**

One recent study reported “Pedestrians who used alcohol were less likely to cross the street in the crosswalk with the signal (22.6% vs 64.7%) and more likely to cross either in the cross walk against the signal (22.6% vs 12.4%) or midblock (54.8% vs 22.8%). Alcohol was also associated with a higher Injury Severity Score (8.82 vs 4.85,  $p < 0.001$ ) and hospital length of stay (3.89 days vs 1.82 days;  $p < 0.001$ ) compared with those with no alcohol involvement.” (Dultz LA et al. Alcohol use by pedestrians who are struck by motor vehicles: How drinking influences behaviors, medical management, and outcomes. 2011 J Trauma 71(5): 1252-1257)

**Wednesday, September 2, 2015****Question:**

ACE inhibitor induced angioedema is well known as an entity that can be severe, resistant to treatment and, in some cases, fatal. Fresh frozen plasma (FFP) has been suggested as a treatment adjunct in the face of severe ACE inhibitor induced angioedema. What is the rationale for the use of FFP in this setting?

**Answer:**

According to the cited reference, “the rationale for the use of FFP is that it provides the enzyme kininase II”. Kininase II catalyzes the degradation of excessive bradykinin; the accumulation of bradykinin is the presumed cause for this form of angioedema via increased vascular permeability due to activation of bradykinin receptors (BKR-2). (Hassen GW, et al. 2013 J Emerg Med 44(4): 764-772)

**Tuesday, September 1, 2015****Question:**

Use of what substance has been implicated as a cause for increased risk of infection in solid organ transplant recipients?

**Answer:**

According to the cited reference, marijuana use has been associated with infection with aspergillus species in post solid organ transplant patients. (Fishman JA Infection in solid-organ transplant recipients. 2007 NEJM 357:2601-2614 and Sakkour A et al. A 56-year-old woman with COPD and multiple pulmonary nodules. Chest 133(2): 566-56)

**Monday, August 31, 2015****Question:**

A variety of concerns have been raised over the safety of bisphosphonates among postmenopausal women for osteoporosis. What is the risk of developing serious atrial fibrillation (requiring hospitalization) associated with the use of bisphosphonates?

**Answer:**

A recent meta-analysis analyzing six (6) observational and six (6) randomized controlled trials suggested “a significantly increased risk of atrial fibrillation requiring hospitalization, but no increase in risk of stroke or cardiovascular mortality, with the use of bisphosphonate”. (Sharma A., et al. Risk of serious atrial fibrillation and stroke with use of bisphosphonates: Evidence from a meta-analysis. 2013 Chest 144(4): 12311-1322)

**Friday, August 28, 2015****Question:**

How have the demographics of heroin use in the United States changed over the past 50 years?

**Answer:**

According to the cited reference “The demographic composition of heroin users entering treatment has shifted over the last 50 years such that heroin use has changed from an inner-city, minority-centered problem to one that has a more widespread geographical distribution, involving primarily white men and women in their late 20s living outside of large urban areas.” This data was based on limited numbers of study subjects and relied on information gleaned from surveys and interviews. Thus the reported results may be limited by the short comings of this methodology, however the data does seem to be supported by reports in the lay press as well as various of governmental studies. (Cicero TJ et al. The changing face of heroin use in the United States- A retrospective analysis of the past 50 years. 2014 JAMA Psych 71(7): 821-826)

**Thursday, August 27, 2015****Question:**

What is cannabidiol and what role is it theorized to play in cannabis related psychosis?

**Answer:**

The cited reference points out that delta tetrahydrocannabinol (THC) is one of 70 phytocannabinoids that can be found in the Cannabis sativa plant and is thought to be the main psychotropic agent of cannabis.” These authors go on to state: “THC is dose dependently associated to psychiatric symptoms such as psychotic like experiences in several studies.” Cannabidiol is one of the phytocannabinoids contained in the cannabis plant. It is theorized that cannabidiol may interfere with (block) the psychomimetic actions of THC, also in a dose dependent fashion. (Schubart CD et al. Cannabidiol as a potential treatment for psychosis. 2014 Eur Neuropsychopharm 24:51-64)

**Wednesday, August 26, 2015****Question:**

Dimethyltryptamine (DMT) is an indolealkylamine hallucinogen. Its agonist action at 5-HT2a, is thought to be primarily responsible for its key psychedelic effects. Why are MAO inhibitor compounds often co-used when DMT is taken for its hallucinogenic effects?

**Answer:**

The cited reference notes “Oral DMT undergoes considerable first-pass metabolism effects from the monoamine oxidase (MAO) enzyme system, necessitating the co-ingestion of a MAO inhibitor...” (Winstock AR et al. Dimethyltryptamine (DMT): Prevalence, user characteristics and abuse liability in a large global sample. 2014 J Psychopharm 28(1): 49-54)



**Tuesday, August 25, 2015**

**Question:**

What substance, derived from the plant *Tabernanthe iboga*, is a naturally occurring alkaloid with hallucinogenic properties and has been advocated by some as an “anti-addiction” drug?

**Answer:**

According to the cited reference, ibogaine has been advocated as a drug that “alleviates drug craving and relapse of drug use in humans...”. However, a variety of reports of adverse effects, including severe QT interval prolongation, have tempered enthusiasm for the development of ibogaine as a drug to be administered for anti-addiction purposes. (Hoelen DWM et al. Long QT syndrome induced by the anti-addiction drug ibogaine. 2009 NEJM 360(3): 308-309)

**Monday, August 24, 2015**

**Question:**

Ayurveda is a traditional system of medicine used by a large percentage of the population of India as well as by large numbers of people worldwide. Ayurvedic medications often include high concentrations of heavy metals that may result in severe toxicity. What is the most likely source for the heavy metal content of Ayurvedic medications?

**Answer:**

While some ayurvedic medications may simply be contaminated by heavy metals, many are the result of the practice known as “*rasa shastra*”. Ayurvedic medications are generally divided into two major categories: herbal only and “*rasa shastra*”. *Rasa shastra* is the ancient practice of deliberately combining herbs with “*bhasmas*” (elaborately prepared metal, mineral, and gem compounds perceived to be safe) with the intention of enhancing therapeutic benefit. These “*bhasmas*” are often responsible for the development of adverse effects. (Saper RB, et al. Lead, mercury, and arsenic in US- and Indian-manufactured Ayurvedic medicines sold via the Internet. 2008 JAMA 300:915 –23.)

**Friday, August 21, 2015**

**Question:**

Thiamine deficiency is a well-known phenomenon in adults with chronic alcohol use. Under what circumstances might infants become afflicted by thiamine deficiency?

**Answer:**

Thiamine is an essential vitamin needed for the normal development of brain tissue in infants and thiamine deficiency in infants is decidedly rare. However in 2003, an outbreak of infantile thiamine deficiency in Israel (9 infants) was reported and was attributed to a defective (thiamine deficient) soy-based infant formula. The cited reference notes “the early clinical symptoms...were non-specific and included gastrointestinal manifestations (vomiting, anorexia, diarrhea, and abdominal distention), neurologic symptoms (lethargy, irritability, and developmental delay) and respiratory symptoms.” (Fattal-Valevski A. et al. Outbreak of life-threatening thiamine deficiency in infants in Israel cause by a defective soy-based formula. 2005 Pediatrics 115(2): e233-e238)

**Thursday, August 20, 2015**

**Question:**

Cases of clinical ergotism have been reported in HIV positive patients being treated with the protease inhibitor ritonavir. What is the mechanism for the development of ergotism in this setting?

**Answer:**

Ritonavir is a strong inhibitor of CYP 3A4 which, when administered with ergotamine and related drugs may alter the metabolism of these drugs and thus may result in elevated blood levels of these drugs and result in potentially severe ergotism. (Ayarragaray J. Ergotism: A change of perspective. 2014 Ann Vasc Surg 28:265-268)

**Wednesday, August 19, 2015**

**Question:**

What is the role of carbamazepine in treating alcohol withdrawal syndrome?

**Answer:**

The cited reference notes “carbamazepine is superior to placebo and equal in efficacy to phenobarbital and oxazepam for patients with mild-to-moderate withdrawal symptoms”. The authors also point out “it reduces emotional distress better and permits a faster return to work than does oxazepam”. Finally carbamazepine is effective in preventing withdrawal seizures and has no potential for abuse. (Kosten TR and O'Connor PG. Management of drug and alcohol withdrawal. 2003 NEJM 348(18):1786-1795)

**Monday, August 17, 2015**

**Question:**

Recent reports described poisoning related to possible palytoxin exposure from live zoanthid coral in home aquariums. Palytoxin, is a potent toxin contained in zoanthid marine corals. What is the mechanism of action of palytoxin and what are the clinical effects associated with exposure to this toxin?

**Answer:**

According to the cited reference, “Palytoxin is a potent vasoconstrictor that acts by binding to Na<sup>+</sup>/K<sup>+</sup> ATPase, which leads to destruction of the ion gradient across cell membranes, passive transport of ions, and ultimately, cell death. It causes a range of effects in animals and humans, depending on the route of exposure. Higher concentrations are required to cause effects following incidental contact depending on whether the exposure occurs through dermal, inhalation, or oral routes. Based on reports in the medical literature and online forums, most aquarium-related exposures occur after subjecting zoanthids to prolonged handling and appear to be related to inhalation or to skin exposures through cuts on the hands and fingers in persons who maintain these types of aquariums. Throughout the Mediterranean region, palytoxin exposure has been linked to fever, conjunctivitis, and respiratory symptoms in persons exposed to marine aerosols during proliferations of palytoxin and palytoxin-like compound-producing marine algae (i.e., algal blooms), but detailed inhalation studies in animal models are lacking. No antidote is available for palytoxin; treatment is supportive.” (Hamade AK et al. ?Suspected Palytoxin Inhalation Exposures Associated with Zoanthid Corals in Aquarium Shops and Homes — Alaska, 2012–2014. MMWR August 14, 2015 / 64(31); 852-855)

**Friday, August 14, 2015**

**Question:**

What are the indicia of a true withdrawal syndrome from any particular substance?

**Answer:**

One authority has proposed that a true withdrawal syndrome “requires evidence that the negative abstinence effects 1) occur reliably, 2) are not exceptionally rare, 3) have a specific time course that includes return to baseline state, 4) abate with re-administration of the drug, 5) are due to deprivation of a specific substance, and 6) are clinically significant.” (Budney AJ et al. Review of the validity and significance of cannabis withdrawal syndrome. 2004 Am J Psychiatry 161:1967-1977)

**Thursday, August 13, 2015**

**Question:**

What is the Clinical Institute Withdrawal Assessment for Alcohol (CIWA) scale?

**Answer:**

CIWA is used to assess alcohol withdrawal symptoms and measures 10 categories of symptoms including agitation, anxiety, auditory disturbances, clouding of sensorium, headache, nausea or vomiting, paroxysmal sweating, tactile disturbances, tremor, and visual disturbances. Very high scores on the CIWA scale predict seizures and delirium. (Kosten TR and O'Connor PG. Management of drug and alcohol withdrawal. 2003 NEJM 348(18):1786-1795)

**Wednesday, August 12, 2015**

**Question:**

What percentage of human cancers in the U.S. are attributable to radiation from CT studies?

**Answer:**

The cited reference notes that as many as 1.5 to 2.0% of all cancers in the US may be attributable to radiation from computerized tomography studies. (Brenner DJ and Hall EJ. Computed tomography- An increasing source of radiation exposure. 2007 NEJM 357:2277-2284)

**Tuesday, August 11, 2015**

**Question:**

Psychotic symptoms are often experienced by users of methamphetamine. Some investigators report that up to 40% of methamphetamine users suffer some degree of psychosis. What are the acute symptoms consistent with methamphetamine induced psychosis?

**Answer:**

The cited reference states "Although transient, in a large proportion of users, acute symptoms can include agitation, violence, and delusions". These authors go on to state "In a subset of individuals, psychosis can recur and persist and may be difficult to distinguish from a primary psychotic disorder such as schizophrenia." (Glasner-Edwards S and Mooney LJ. Methamphetamine psychosis: Epidemiology and management. 2014 CNS Drugs 28: 1115-1126)

**Monday, August 10, 2015**

**Question:**

Tranexamic acid (TXA) is an amino acid analogue of lysine that inhibits the activation of the fibrinolytic enzyme plasmin. The use of this agent to reduce bleeding in trauma patients was pioneered in the military. One important study (known as CRASH-2) demonstrated a 15% reduction in relative risk of death due to bleeding in civilian trauma patients associated with the use of TXA. What are the most serious potential side effect of TXA?

**Answer:**

According to the cited reference, TXA "antagonizes GABA and glycine receptors in the CNS, reducing seizure threshold." However, this effect appears to be dose related. Postoperative seizures have been observed in patients receiving TXA but not reported in trauma patients receiving TXA. (Heier HE et al. Use of tranexamic acid in bleeding combat casualties. 2015 Military Med 180(8):844-846)

**Friday, August 7, 2015**

**Question:**

Foam sclerosants are often used in the elective treatment of varicose veins. These agents are injected into the target vein and result in thrombus formation and venous occlusion. What are the serious complications that have been associated with the use of foam sclerosants?

**Answer:**

According to the cited reference "Use of foam sclerosants has been associated with a risk of intracerebral gas emboli, which can result in neurologic adverse events, including stroke, migraine, and visual disturbances." (The Medical Letter, August 3, 2015, 57(1474):111-112)

**Friday, August 7, 2015**

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**Thursday, August 6, 2015**

**Question:**

The first well-documented outbreak of methylmercury poisoning by consumption of contaminated fish occurred in Minamata, Japan in 1953. This outbreak resulted in poisoning, often referred to as Minamata Disease, in over 2000 individuals. What visual problem was observed in all cases of Minamata Disease as a result of this tragic methylmercury exposure?

**Answer:**

According to the cited reference, "A conspicuous feature of the disease (Minamata Disease) is bilateral and symmetric concentric constriction of the visual fields". (Ekino S et al. Minamata Disease revisited: An update on the acute and chronic manifestations of methyl mercury poisoning. 2007 J Neurol Sci 262:131-144)

**Wednesday, August 5, 2015**

**Question:**

A strong association between some occupational exposures to vinyl chloride and angiosarcoma of the liver has been widely discussed in the medical literature. How many cases of angiosarcoma of the liver are diagnosed each year in the United States and what percentage of cases of angiosarcoma of the liver are not associated with any known etiologic factors?

**Answer:**

According to the cited references only 10-20 case of angiosarcoma of the liver are diagnosed each year in the US and 75 % of all angiosarcomas "are not associated with any known etiologic factors." (Mani H et al. Mesenchymal tumors of the liver. 2001 Clin Liver Dis 5:219-257 and Falk H et al. Epidemiology of hepatic angiosarcoma in the United States: 1964-1974. 1981 Env Health Perspect 41:107-113 as cited in Ananthakrishnan A et al. Epidemiology of primary and secondary liver cancers. 2006 Sem Interventional Radiol 23(1): 47-63)

**Tuesday, August 4, 2015**

**Question:**

What is anandamide?

**Answer:**

Anandamide was the first endocannabinoid agonist to be identified; it is the ethanolamine of arachidonic acid. The name "anandamide" is derived from the Sanskrit word "ananda" which means "overjoy" or "bliss". (Pamplona FA and Takahashi RN. Psychopharmacology of the endocannabinoids: far beyond anandamide. 2012 J Psychopharm 26(1): 7-22)

**Friday, July 31, 2015**

**Question:**

Most benzodiazepines are metabolized, at least to some degree, by CYP 3A4. Which benzodiazepines are not metabolized by CYP 3A4?

**Answer:**

Lorazepam, oxazepam and temazepam are not metabolized by CYP 3A4. (The Medical Letter July 6, 2105, 57(1472):95-98)

**Thursday, July 30, 2015**

**Question:**

What is the utility of platelet factor 4-heparin antibody tests in patients with possible heparin induced thrombocytopenia?

**Answer:**

According to the cited reference "Platelet factor 4- heparin antibody tests should be ordered only if clinical features reasonably suggest heparin induced thrombocytopenia. These tests have a high negative predictive value but a low positive predictive value." (Greinacher A. Heparin-induced thrombocytopenia. 2015 NEJM 373(3): 252-261)

**Wednesday, July 29, 2015**

**Question:**

What is the STRIDE database?

**Answer:**

"STRIDE" stands for the "System to Retrieve Information from Drug Evidence". It is a database of drug exhibits sent to DEA labs for analysis from DEA, other Federal agencies, and some local law enforcement agencies. DEA established this on-line data set to provide ready access to drug seizure data. DEA shares these data with researchers, academics, policymakers, and others to provide an understanding of drug availability. (<http://www.dea.gov/resource-center/stride-data.shtml>; accessed July 2015)

**Tuesday, July 28, 2015**

**Question:**

How does absorption, onset of effects, duration of intoxication and mean peak THC plasma concentration differ between smoked marijuana and ingested marijuana?

**Answer:**

The cited reference notes "...absorption is slower, the onset of effects is delayed (with mean peak plasma concentration at 1–2 hours after ingestion, in contrast with 5–10 minutes to peak plasma concentrations if smoked), and duration of intoxication is longer when THC is ingested compared with when it is smoked." (Perez-Reyes M, et al. Pharmacology of orally administered 9-tetrahydrocannabinol. 1973 Clin Pharmacol Ther 14:48–55 as cited in Hancock-Allen JB et al. Notes from the Field: Death Following Ingestion of an Edible Marijuana Product — Colorado, March 2014. July 24, 2015 MMWR 64(28); 771)

**Monday, July 27, 2015**

**Question:**

Determining the epidemiology of inhalant abuse is difficult and has been essentially defined most effectively by several population surveys. Which surveys have been most informative regarding the abuse of inhalants?

**Answer:**

The Monitoring the Future (MTF) survey, the Youth Risk Behavior Survey (YRBS) and the National Survey on Drug Use and Health (NSDUH) have been the most informative population surveys regarding the use of inhalants. (Howard MO et al. Inhalant abuse and inhalant use disorders in the United States. 2011 Add Sci Clin Prac 23:18-31)

**Friday, July 24, 2015**

**Question:**

What is the mechanism of action for the smoking cessation drug varenicline?

**Answer:**

The cited reference points out "Varenicline is a partial agonist binding with high affinity and selectivity at alpha4beta2 neuronal nicotinic acetylcholine receptors." (Ebbert JO et al. Effect of varenicline on smoking cessation through smoking reduction: A randomized clinical trial. 2015 JAMA 313(7): 687-694)

**Thursday, July 23, 2015**

**Question:**

What is the phenomenon known as "dose dumping" and which commonly ingested substance is often responsible for this potentially serious safety concern??

**Answer:**

According to the cited reference "dose dumping" involves "unintended, rapid drug release in a short period of time of the entire amount or a significant fraction of the drug contained in a modified release dosage form". This phenomenon specifically relates to "alcohol-induced dose dumping" described as: "The concomitant intake of alcoholic beverages together with oral controlled-release opioid formulations poses a serious safety concern since alcohol has the potential to alter the release rate controlling mechanism of the dosage form which may result in an uncontrolled and immediate drug release."(Meyer RJ and Hussain AS. Awareness Topic: Mitigating the risks of ethanol induced dose dumping from oral sustained/controlled release dosage forms, in: ACPs Meeting October, 2005, as cited in Jedinger N et al. The design of controlled-release formulations resistant to alcohol-induced dose dumping- A review. 2014 Eur J Pharm Biopharm 87:217-226)

**Wednesday, July 22, 2015**

**Question:**

Methadone has been recognized as one of the many drugs capable of prolongation of the rate-corrected QT interval (QTc) of the EKG. This is considered to be a marker for risk for the potentially fatal arrhythmias including torsades des pointes. What is current recommendation regarding the utility of EKG screening aimed at preventing QTc prolongation related cardiac arrhythmias in methadone treated opioid dependent individuals?

**Answer:**

A recent report from the Cochrane Collaboration reports “no evidence has been found to support the use of the ECG for preventing cardiac arrhythmias in methadone treated opioid dependents.” (Pani PP et al. QTc interval screening for cardiac risk in methadone treatment for opioid dependence. 2013 Cochrane Database of Systematic Reviews, issue 6 Art. No. CD008939. DOI: 10.1002/14651858.CD008939.pub2)

**Tuesday, July 21, 2015**

**Question:**

What is REMS?

**Answer:**

REMS stands for “Risk Evaluation and Mitigation Strategy” and applies to extended release (ER) and long-acting (LA) opioid medications. The REMS is part of a multi-agency Federal effort to address the growing problem of prescription drug abuse and misuse. The REMS introduces new safety measures to reduce risks and improve safe use of ER/LA opioids while continuing to provide access to these medications for patients in pain. All ER/LA opioid analgesics will be required to have a REMS because FDA has concluded that there is a disproportionate safety problem associated with these products that must be addressed. (<http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm163647.htm>; accessed July 2015)

**Monday, July 20, 2015**

**Question:**

What hallucinogen has been used to treat the “semi-magical disease known as panzon de Borrego, or swollen belly”, believed (by the Mazatec Indians of Oaxaca, Mexico), to be caused by an evil sorcerer?

**Answer:**

Salvia divinorum, a member of the mint family, contains Salvinorin A, and this plant has been used by Shamans of the Mazatec Indians for centuries to treat a variety of maladies including headache, diarrhea, anemia and “panzon de Borrego”. (Zawilska JB and Wojcieszak J. Salvia divinorum: from Mazatec medicinal and hallucinogenic plant to emerging recreational drug. 2013 Hum Psychopharm Clin Exp 28:403-412)

**Friday, July 17, 2015**

**Question:**

What is the so-called “gateway hypothesis” of drug use?

**Answer:**

The cited article notes the “gateway hypothesis” describes the fact that “in the general population of the United States and other Western societies, a well defined developmental sequence of drug use occurs that starts with a legal drug and proceeds to illegal drugs. Specifically, the use of tobacco or alcohol precedes the use of marijuana, which in turn precedes the use of cocaine and other illicit drugs.” (Kandel ER and Kandel DB. 2014 NEJM 371: 932-943)

**Thursday, July 16, 2015**

**Question:**

What is the nature and time course of methamphetamine withdrawal?

**Answer:**

The cited reference notes that “methamphetamine withdrawal syndrome [is] characterized principally by increases in sleeping and appetite with an early cluster of depression related symptoms including inactivity, fatigue, anhedonia and dysphoria”. The cited report further concluded “This study has provided evidence of a methamphetamine withdrawal syndrome that can be categorized into two phases, the acute phase lasting 7-10 days during which overall symptom severity declined in a linear pattern from a high initial peak and a sub-acute phase lasting at least a further 2 weeks.” (McGregor C. et al. The nature, time course and severity of methamphetamine withdrawal. 2005 Addiction 100(9): 1320-1329)

**Wednesday, July 15, 2015**

**Question:**

What are the cited motives for patients who report using synthetic cannabinoids?

**Answer:**

One study recently evaluated the motives for synthetic cannabinoid use and reported 91% of persons used out of “curiosity” while 89% used “to feel good or get high” and 71% used “to get high without risking a positive drug test”. (Bonar EE et al. Synthetic cannabinoid use among patients in residential substance use disorder treatment: prevalence, motives, and correlates. 2014 Drug Alc Depend 143:268-271 as cited in Trecki J et al. Synthetic cannabinoid-related illness and deaths. 2015 NEJM 373(2): 103-107)

**Tuesday, July 14, 2015**

**Question:**

UVA type solar ultraviolet radiation is the form of ultraviolet radiation most closely associated with the development of skin cancer. Sunscreen products are touted as one of the best ways to interfere with over exposure to UVA radiation. What are the primary constituents of broad-spectrum sunscreens in the US today intended to block UVA?

**Answer:**

The cited reference notes that “Most broad-spectrum sunscreens marketed in the United States contain oxybenzone or avobenzone to block the type of ultraviolet radiation, known as UVA...”. (Sharfstein JM. A spotlight on sunscreen regulation. 2015 NEJM 373(2): 101-103)

**Monday, July 13, 2015**

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**Question:**

With regard to extra corporeal removal of toxicants, the clearance of what molecule is used to describe the high flux dialysance of a given dialysis membrane?

**Answer:**

According to the cited reference, the clearance of beta-2 microglobulin is often used "to express the high flux dialysance of a membrane". (Garlich FM and Goldfarb DS. Have advances in extra corporeal removal techniques changed the indications for their use in poisonings? 2011 Adv Chronic Kidney Dis 18(3):172-179) r

**Friday, July 10, 2015**

**Question:**

What are PDMPs?

**Answer:**

PDMPs are "prescription drug monitoring programs". According to the cited reference, PDMPs are "state administered databases that collect, store, and distribute data on controlled substance prescribing. Authorized users- prescribers, pharmacists, and/or law enforcement, depending on individual state laws- access these databases in order to track and change prescribing patterns." (Gugelmann H et al. Windmills and pill mills: Can PDMPs tilt the prescription drug epidemic? 2012 J Med Toxicol 8:378-386)

**Thursday, July 9, 2015**

**Question:**

The symptoms of methamphetamine-induced psychosis are generally similar to those symptoms manifested in schizophrenia. What are the most frequently reported symptoms in cases of methamphetamine-induced psychosis?

**Answer:**

According to the cited reference, the most frequently reported symptoms in cases of methamphetamine-induced psychosis are "delusions of persecution and auditory hallucinations". (Rusniak DE. Neurologic manifestations of chronic methamphetamine abuse. 2013 Psychiatr Clin N Amer 36:261-275)

**Wednesday, July 8, 2015**

**Question:**

Long-term smokers are generally considered to have some level of respiratory impairment. How many smokers have one or more respiratory-related impairments yet demonstrate normal spirometry?

**Answer:**

According to the cited reference, more than 54% of smokers with normal spirometry will have one or more respiratory-related impairments. (Regan EA et al. Clinical and radiologic disease in smokers with normal spirometry. 2015 JAMA Intern Med published online June 15, 2015 doi:10.1001/jamainternmed.2015.2735)

**Tuesday, July 7, 2015**

**Question:**

Colchicine has been used in the treatment of gout and familial Mediterranean fever. What are the plants from which colchicine is extracted?

**Answer:**

Colchicine is extracted from the autumn crocus (Colchicine autumnale) and the glory lily (Gloriosa superba). Finkelstein Y et al. Colchicine Poisoning: the dark side of an ancient drug. 2010 Clin Tox 48(5): 407-414)

**Monday, July 6, 2015**

**Question:**

A withdrawal syndrome related to methamphetamine has been identified. What characterizes the time course of methamphetamine withdrawal?

**Answer:**

The cited reference reports "Methamphetamine withdrawal severity declined from a high initial peak within 24 hours of the last use of amphetamines reducing to near control levels by the end of the first week of abstinence (the acute phase). The acute phase of amphetamine withdrawal was characterized by increased sleeping and eating, a cluster of depression-related symptoms and less severely, anxiety and craving-related symptoms. Following the acute withdrawal phase most withdrawal symptoms remained stable and at low levels for the remaining 2 weeks of abstinence." (McGregor C et al. The nature, time course and severity of methamphetamine withdrawal. 2005 Addiction. 100(9):1320-1329)

**Friday, July 3, 2015**

**Question:**

A number of informative studies have reported on the epidemiology of inhalant use/abuse. These include the "Monitoring the Future" survey, the "Youth Risk Behavior Study" and the "National Survey on Drug Use and Health". What do these studies reveal about the "ever-use" of inhalants to "get high" in the United States population?

**Answer:**

The cited reference notes that the above mentioned studies report: "an estimate 9 % of the US population age 12 and older (22.5 million people) have used an inhalant for its psychoactive properties at least once". (Howard MO et al. Inhalant use and inhalant use disorders in the United States. 2011 Addiction Sci Clin Practice 6(1): 18-31)

**Thursday, July 2, 2015**

**Question:**

There are currently three approved SGLT-2 (sodium-glucose co-transporter-2) inhibitors; canaglifozin (Invokana, Invokamet), dapaglifozin (Farxiga, Xigduo XR), and empaglifozin (Jardiance, Glyxambi). The FDA has warned that the use of these medications can cause what serious complication usually associated with type 1 diabetes?

**Answer:**

SGLT-2 (sodium-glucose co-transporter-2) inhibitors have been implicated in causing roughly 20 reported cases of diabetic ketoacidosis (DKA). Typically, DKA occurs in type 1 diabetics where as the cases associated with SGLT-2 inhibitors were reported in type 2 diabetics. The cited reference reports that about 50% of these cases were not associated with the precipitation factors usually found in DKA including “infection, reduced caloric intake or reduced insulin dose”. The cited reference also notes “The mechanism by which these drugs could cause ketoacidosis has not been established”. (The Medical Letter June 22, 2015, 57(1471): 94)

**Wednesday, July 1, 2015****Question:**

What is the mechanism of action of ketamine?

**Answer:**

According to the cited reference, “ketamine is a dissociative agent acting through antagonism of glutamate N-methyl-D-aspartate receptors, which causes a trance-like state resulting in analgesia and amnesia”. (Hopper AB et al. Ketamine use for acute agitation in the emergency department. 2015 J Emerg Med 4896): 712-719)

**Tuesday, June 30, 2015****Question:**

What organism is responsible for the majority of recreational water-associated outbreaks of illness in the United States?

**Answer:**

According to the cited reference, “Cryptosporidium continues to be the dominant etiology of recreational water-associated outbreaks. Half of all treated recreational water-associated outbreaks reported for 2011–2012 were caused by Cryptosporidium. Among treated recreational water-associated outbreaks of gastrointestinal illness that began in June–August, >90% were caused by Cryptosporidium, an extremely chlorine-tolerant parasite that can survive in water at CDC-recommended chlorine levels (1–3 mg/L) and pH (7.2–7.8) for >10 days.” (MMWR. Outbreaks of Illness Associated with Recreational Water — United States, 2011–2012. June 26, 2015 / 64(24): 668-672)

**Monday, June 29, 2015****Question:**

Why has the drug disulfiram been considered in the treatment of chronic cocaine dependence?

**Answer:**

The cited study notes “Disulfiram has shown promise as a pharmacotherapy for cocaine dependence in clinical settings, although it has many targets, and the behavioral and molecular mechanisms underlying its efficacy are unclear. One of many biochemical actions of disulfiram is inhibition of dopamine beta-hydroxylase (DBH), the enzyme that converts dopamine (DA) to norepinephrine (NE) in noradrenergic neurons. Thus, disulfiram simultaneously reduces NE and elevates DA tissue levels in the brain.” These effects might tend to attenuate adverse cocaine effects related to dopamine depletion. (Cooper DA et al. Effects of pharmacologic dopamine beta-hydroxylase inhibition on cocaine-induced reinstatement and dopamine neurochemistry in squirrel monkeys. 2014 J Pharm Exp Therapeutics 35091): 144-152)

**Friday, June 26, 2015****Question:**

Which antibiotics have been reported to cause false positive opiate urine drug screens?

**Answer:**

Fluoroquinolones (with levofloxacin, ofloxacin and pefloxacin being the most common fluoroquinolones associated with such cross reactions) and rifampin have been reported to cause false positive urine drug screens for opiates by cross reactivity. Shafiq Q and Mutgi A. Urine opiate screening: false positive result with levofloxacin. 2010 CMAJ 182(15): 1644-1645

**Thursday, June 25, 2015****Question:**

Acute and chronic poisoning with selenium or selenium containing products has been associated with a strong “garlic-like” odor of the breath in some cases. What is the presumed cause for this odor?

**Answer:**

The cited reference notes: “The strong garlic-like odor usually present in both acute and chronic [selenium] poisoning is attributed to the volatile metabolite dimethylselenide. (Barceloux DG Selenium. 1999 J Tox Clin Tox 37:145-172 as cited in Nuttall KL. Evaluating selenium poisoning. 2006 Ann Clin Lab Sci 36(4): 409-420)

**Wednesday, June 24, 2015****Question:**

What is the death rate associated with delirium tremens (alcohol withdrawal delirium)?

**Answer:**

The cited reference notes “Approximately 1 to 4% of hospitalized patients who have withdrawal delirium (DTs) die.” They go on to state that “this rate could be reduced if an appropriate and timely diagnosis were made and symptoms were adequately treated. (Schuckit MA. Recognition and management of withdrawal delirium (delirium tremens) 2014 NEJM 371:2109-2113)

**Tuesday, June 23, 2015****Question:**

The cited reference notes that “Marchiafava–Bignami disease (MBD) was originally described as a rare, fatal disease affecting wine drinkers.” What is the pathophysiology of MBD?

**Answer:**

The cited reference notes that MBD is “Characterized by demyelination and necrosis of the corpus callosum, it has long been considered to be of either a toxic or nutritional etiology.” The authors go on to state that “Marchiafava–Bignami disease (MBD) is a rare condition mainly associated with alcoholism, although it may be mimicked by several other disorders that cause corpus callosum lesions” and “As thiamine deficiency is frequently associated with alcoholism, malnutrition and prolonged vomiting; we recommend prompt treatment of MBD with parenteral thiamine in such subjects.” (Hillbom M, et al. Diagnosis and management of Marchiafava-Bignami disease: A review of CT/MRI confirmed cases. 2014 J Neurol Neurosurg Psych 85:168-173)

**Monday, June 22, 2015****Question:**

What is the utility of carbohydrate-deficient transferrin (CDT) with regard to alcohol use disorder?

**Answer:**

The cited reference notes that CDT “is an indicator for long-term alcohol consumption. Daily intake of alcohol exceeding 50-80 grams ethanol for periods longer than 2 weeks results in increased levels of CDT..... After discontinuing drinking, the serum CDT level usually normalizes within approximately 2-4 weeks..... (Hock B et al. Validity of carbohydrate-deficient transferrin (CDT), gamma glutamyltransferase and mean corpuscular erythrocyte volume as biomarkers for chronic alcohol abuse. 2005 Addiction 100(1): 1477-1486)

**Friday, June 19, 2015****Question:**

What is the relationship between ingested acetaminophen dose and the development of nephrotoxicity?

**Answer:**

The authors of the cited reference state, “The relationship between dose and nephrotoxicity is not as clearly delineated as with that of APAP-induced hepatotoxicity. APAP-induced nephrotoxicity may occur at lower doses than that seen with hepatotoxicity. In 1 of 2 limited poison center retrospective series, almost one third of patients developed renal insufficiency in the absence of significant hepatotoxicity.” (Mazer M and Perrone J. Acetaminophen-induced nephrotoxicity: Pathophysiology, clinical manifestations and management. 2008 J Med Tox 4(1): 2-6 and Von Mach MA et al. Experiences of a poison center network with renal insufficiency in acetaminophen overdose: an analysis of 17 cases. 2005 Clin Tox 43: 31-37)

**Thursday, June 18, 2015****Question:**

How does the decrement in pulmonary function differ between marijuana smokers and tobacco smokers?

**Answer:**

In contrast to tobacco exposure, the association between marijuana exposure and pulmonary function is nonlinear. In addition, the authors of the cited study point out that “Occasional and low cumulative marijuana use was not associated with adverse effects on pulmonary function.” (Pletcher M. et al. Association between marijuana exposure and pulmonary function over 20 years. 2012 JAMA 307(2): 173-181)

**Wednesday, June 17, 2015****Question:**

What is “NASPER”?

**Answer:**

“NASPER” is the National All Schedules Prescription Electronic Reporting Act. This Act was passed in 2005 with the aim of providing Federal support to states for prescription monitoring programs (PMPs). It is the only statutorily authorized program to assist states in combating prescription drug abuse of controlled substances through a prescription monitoring program. To date 38 states have PMPs, but there is a significant difference in the manner and frequency with which the data is collected. (<http://nasper.org/Documents/FactSheet-DrugAbuse-2011.pdf>; accessed June 2015)

**Tuesday, June 16, 2015****Question:**

In 2010 the FDA approved a reformulation of the drug OxyContin (street names “80’s”, “Beans”, “OC”, “Orange Crayons”). What was the goal of the reformulation of OxyContin and what was one important unintended effect of this reformulation?

**Answer:**

The reformulation of OxyContin made it more difficult for the pill to be broken down for injection, snorting, and smoking. It is posited that this reformulation of OxyContin contributed to an increase in heroin use. (<http://www.dea.gov/resource-center/dir-ndta-unclass.pdf>; accessed June 2015)

**Monday, June 15, 2015****Question:**

How do the peak withdrawal symptoms associated with buprenorphine compare with those associated with methadone or heroin?

**Answer:**

According to the cited reference, “Buprenorphine has milder peak withdrawal symptoms than does methadone; the duration of symptoms is intermediate between those for methadone and those for heroin”. (Kosten TR and O’Connor PG. Management of drug and alcohol withdrawal. 2003 NEJM 348(18):1786-1795)

**Friday, June 12, 2015****Question:**

Heroin associated myelopathy has been reported. What are the suggested mechanisms for the development of this uncommon complication of heroin use?



**Answer:**

The cited reference notes “Suggested mechanisms of heroin-associated myelopathy include hypotension, a direct toxic effect of heroin, vasculitis, and hypersensitivity reaction.” These authors go on to discuss: “Hypersensitivity has been the predominant theory since the initial reports, as most patients who developed myelopathy had relapsed into heroin use after a period of abstinence. As with many drug allergies, sensitization must occur first. Upon re-exposure to the drug, a hypersensitivity reaction ensues.” (McCreary M et al. Acute myelopathy following intranasal insufflation of heroin: A case report. 2000 Neurology 55(2): 316-317)

**Thursday, June 11, 2015****Question:**

During the early 1970s babies bathed in a phenolic derivative particularly effective against Gram-positive organisms resulted in severe central nervous system effects. What was the substance these babies were bathed in and what were the severe CNS effects that resulted?

**Answer:**

Hexachlorophane was the material used to bath the babies in the reference cases. This substance is absorbed through intact skin and resulted in the development of spongiiform myelinopathy and encephalopathy. (Shuman RM et al. Neurotoxicity of hexachlorophene in humans. I. A clinicopathologic study of 248 children. 1974 Pediatrics 54:689-695)

**Wednesday, June 10, 2015****Question:**

What is the so-called “Jack Rabbit” field experiment?

**Answer:**

The “Jack Rabbit” field experiment, conducted at the Dugway Proving Ground in 2010, involved controlled releases of pressurized liquefied chlorine and ammonia into a depression in the ground. The dispersion characteristics of the resultant chemical plumes were studied and described. These experiments provide important modeling information with regard to chemical releases from both accidental and intentional events. (Hanna S et al. The Jack Rabbit chlorine release experiments: implications of dense gas removal from a depression and downwind concentrations. 2012 J Hazardous Materials 213-214:406-412)

**Tuesday, June 9, 2015****Question:**

What are so-called “burn pits”? What are the potential adverse health consequences associated with burn pits?

**Answer:**

Burn pits are open-air waste burning locations often used by deployed military personnel when other waste disposal options are not available. The U.S. military has utilized burn pits in both Afghanistan and Iraq until their use was restricted in 2009. However, burn pits continue to be used in Afghanistan as recently as January 2011. Due to the potential for generation of toxic pyrolysis products and the potential for human exposure, the Institute of Medicine has recently studied burn pit exposures for military personnel. The US Army Public Health Command recently reported that the “risks of acute health effects of all chemicals detected, except coarse particulate matter (PM) was low and that long term health risks were “acceptable”. (“Featured for the Institute of Medicine”: Long-term health consequences of exposure to burn pits in Iraq and Afghanistan. 2015 Military Medicine 180(6): 601-603)

**Monday, June 8, 2015****Question:**

What are the generally recognized toxicologic causes of angiosarcoma of the liver?

**Answer:**

The generally recognized toxicologic causes of angiosarcoma of the liver include (in no particular order) vinyl chloride, thorium dioxide (Thorotrast), arsenic and anabolic steroids. (Heath CW et al. Characteristics of cases of angiosarcoma of the liver among vinyl chloride workers in the United States. 1975 Ann NY Acad Sci 246:231-236)

**Friday, June 5, 2015****Question:**

What is the best method for decontamination of the skin following dermal exposure to phenol?

**Answer:**

The cited reference notes: “Removing a person from phenol exposure is the most important method for reducing toxic effects of phenol. This is especially important following dermal exposure, after which speed in removing phenol from the skin is important. Because a study has shown that dilution in water increases the dermal absorption of phenol, it has been recommended that polyethylene be used to remove dermal contamination with phenol. Because water is readily available, others believe that its use is more appropriate for the decontamination of skin following phenol exposure. A study is available that evaluated several strategies to decontaminate the skin of pigs following acute dermal exposure to phenol. The study showed that polyethylene glycol (PEG 400) and 70% isopropanol were superior to other treatments and equal effective in reducing skin damage induced by phenol.” (<http://www.atsdr.cdc.gov/toxprofiles/tp115-c3.pdf>; accessed May 2015)

**Thursday, June 4, 2015****Question:**

What are the constituents of concentrated laundry detergent packs currently marketed in the U.S.?

**Answer:**

According to the cited reference, “US products may contain anionic surfactants (15%-60%), nonionic surfactants (10%-30%), benzenesulfonic acid derivatives (0%-30%), propylene glycol (0%-15%), and polymers (3% -7%). U.S. product formulations vary by brand. (Yin S et al. Laundry pack exposures in children 0-5 years evaluated at a single pediatric institution. 2015 J Emerg Med 48(5): 566-572)

**Wednesday, June 3, 2015**

**Question:**

When compared with methadone maintenance, what are the general advantages of using buprenorphine in the outpatient treatment of opiate addicted individuals?

**Answer:**

The cited reference reports "Buprenorphine, an opioid partial agonist, has appeal for many opiate-dependent individuals because of the convenience of monitoring and the decreased stigma of receiving it in a general medical office setting." (Liebschutz JM et al. Buprenorphine treatment for hospitalized, opioid-dependent patients a randomized clinical trial. 2014 JAMA Int Med 174(8): 1369-1376)

**Tuesday, June 2, 2015**

**Question:**

With regard to street drugs, adulterants are "pharmacologically active ingredients added to give either synergistic or antagonistic effects" to the original drug of abuse. Which adulterant, sometimes added to cocaine and or crack cocaine, has been specifically linked to renal injury?

**Answer:**

Phenacetin, an analgesic drug banned for use in the early 1980s, has been found as a cocaine adulterant and this drug can cause renal injury (renal papillary necrosis) (Cole C. et al "Cut. A Guide to Adulterants, Bulking Agents and other Contaminants Found in Illicit Drugs" (<http://www.scribd.com/doc/79305591/CUT-A-guide-to-Adulterants#scribd>; accessed May 2015)

**Monday, June 1, 2015**

**Question:**

Why are pregnant females encouraged to avoid taking NSAIDs?

**Answer:**

Pregnant females are encouraged to avoid taking NSAIDs, especially during the third trimester, due to concern for premature (in utero) closure of the ductus arteriosus (DA). The authors of the cited reference go on to describe "Premature closure of the DA in utero is a rare but well- recognized condition. It can occur spontaneously or secondary to the use of prostaglandin synthetase inhibitors such as NSAIDs and glucocorticoids. In utero DA constriction also has been described in association with indometacin tocolysis of preterm labor. A dramatic increase in the incidence of DA constriction after 31 weeks gestation indicates that the DA is more sensitive to constricting factors in the latter weeks of pregnancy." (Shastri A et al. Maternal diclofenac medication in pregnancy causing in utero closure of the fetal ductus arteriosus and hydrops. 2013 Pediatr Cardiol 34:1925-1927)

**Friday, May 29, 2015**

**Question:**

When Clostridium difficile colonizes the large intestines two protein exotoxins are released. What are these exotoxins? Why do infants colonized with C. difficile not develop symptomatic disease?

**Answer:**

According to the cited reference, "C. difficile colonizes the large intestine and releases two protein exotoxins (TcdA and TcdB) that cause colitis in susceptible persons." The authors of the cited reference note "Symptoms of colitis do not develop in all colonized persons. For example, the majority of infants are colonized with C. difficile but are asymptomatic, possibly owing to the lack of toxin-binding receptors in the infant gut, as shown in animal models and as suggested by the common development of antibodies to C. difficile toxins in infants without clinical infection." (Leffler DA and Lamont JT. Clostridium difficile infection. 2015 NEJM 372(16): 1539-1548)

**Thursday, May 28, 2015**

**Question:**

Historically, the topical application of silver sulfadiazine has been avoided in very young infants. What is the reason for this?

**Answer:**

According to the cited reference, "Historically, treatment with silver sulfadiazine was regarded with caution due to its association with kernicterus. The sulfur component in these older products binds with albumin, resulting in excess unbound bilirubin that readily crosses the blood brain barrier. However some argue that these complications may be exacerbated by the chlorhexidine component of the silver sulfadiazine dressing causing additional toxicity." (Rustogi R. et al. The use of Acticoat in neonatal burns. 2005 Burns 31(7): 878-882 as cited in August DL et al, Silver based dressing in an extremely low birth weight infant. 2015 J Wound Ostomy Continence Nurs 42(3): 290-293)

**Wednesday, May 27, 2015**

**Question:**

Methotrexate related central nervous system (CNS) toxicity is likely related to CNS folate homeostasis. Some have proposed the use of dextromethorphan administration for patients suffering subacute methotrexate toxicity. What is the basis for the use of dextromethorphan in this setting?

**Answer:**

The cited reference notes: "The use of folinate rescue has been described to decrease toxicity in patients who had received intrathecal methotrexate. It has also been described in previous studies that there is an elevated level of homocysteine in plasma and cerebrospinal fluid of patients who had received intrathecal methotrexate. Homocysteine is an N-methyl-D-aspartate receptor agonist." The authors of the cited study discuss the use of dextromethorphan as follows: "The use of dextromethorphan, noncompetitive N-methyl-D-aspartate receptor antagonist, has been used in the treatment of sudden onset of neurological dysfunction associated with methotrexate toxicity." These authors report: "The use of dextromethorphan in most of our patients resulted in symptomatic improvement. In this patient population, earlier administration of dextromethorphan resulted in faster improvement of impairments and led to prevention of recurrence of seizure activity induced by methotrexate." (Afshar M et al. Review of dextromethorphan administration in 18 patients with subacute methotrexate central nervous system toxicity. 2014 Pediatr Neurol 50:625-629)

**Tuesday, May 26, 2015**

**Question:**

What is the Hawthorne Effect?

**Answer:**

According to the cited reference: “The Hawthorne effect is one of the most famous effects in sociological studies. It means that subjects alter an aspect of their behavior when they realize that they are being studied, and the change is not in response to any particular intervention. The term was coined in 1950 by Henry A. Landsberger in the analysis of experiments from 1924 to 1932 at the Hawthorne Works (a Western Electric factory outside Chicago, IL). Hawthorne Works had commissioned a study to see if its workers would become more productive with higher levels of lighting. Initially, it was thought that workers' productivity improved with better lighting, but later, it was shown that the observed improvement in productivity was unrelated to levels of light. It was suggested that the productivity gain occurred because of the motivational effect on the workers as a result of the interest being shown in them rather than changes in the level of lighting.” (Oh MA and Uribarri J. What can we learn from the saga of chitosan gums in hyperphosphatemia therapy? Clin J Am Soc Nephrology 9(5): 967-970)

**Monday, May 25, 2015****Question:**

What are the ATSDR's so-called “Interaction Profiles”?

**Answer:**

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) mandates that the ATSDR shall assess whether adequate information on health effects is available for the priority hazardous substances. Where such information is not available or under development, ATSDR shall, in cooperation with the National Toxicology Program, initiate a program of research to determine these health effects.

To carry out this legislative mandate, ATSDR's Division of Toxicology and Human Health Sciences (DTHHS) has developed a chemical mixtures program. As part of the mixtures program, ATSDR developed a guidance manual that outlines the latest methods for mixtures assessment. In addition, a series of documents called Interaction Profiles are being developed for certain priority mixtures that are of special concern to ATSDR. The purpose of the Interaction Profile is to evaluate data on the toxicology of the 'whole' priority mixture (if available) and on the joint toxic action of the chemicals in the mixture in order to recommend approaches for the exposure-based assessment of the potential hazard to public health. (<http://www.atsdr.cdc.gov/interactionprofiles/index.asp>; accessed May 2015)

**Friday, May 22, 2015****Question:**

What is hexamethylene diisocyanate (HDI) and what are the adverse health effects that may be associated with chronic, high dose exposure to this chemical?

**Answer:**

Hexamethylene diisocyanate is a pale yellow liquid with a strong odor. It is an industrial chemical that is not known to occur naturally. It is also commonly known as HDI, 1,6-hexamethylene diisocyanate, 1,6-diisocyanatohexane, Mondur HX, and Desmodur H. Hexamethylene diisocyanate is mainly used to make polyurethane foams and coatings. It is also used as a hardener in automobile and airplane paints. According to the cited reference: [some] “People exposed to hexamethylene diisocyanate for a long time (a few months to a few years) have shown an allergic, asthma-like syndrome. The symptoms consist of shortness of breath, wheezing, bronchitis, and coughing. These symptoms are not usually seen when the person is not using a product that contains hexamethylene diisocyanate, but will start up again when they begin to use hexamethylene diisocyanate products again.” (<http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=874&tid=170#bookmark06>; accessed April 2015)

**Thursday, May 21, 2015****Question:**

During the late 1970s the drug dipyrone (metamizole) was banned by the FDA. Despite being banned this drug is still widely used in the US. What is the primary toxicity of this drug and why is it still found in the US despite the FDA ban?

**Answer:**

Dipyrone is a nonsteroidal drug that was banned due to its association with the development of myelotoxicity (specifically agranulocytosis). The incidence of myelotoxicity induced by dipyrone is reportedly approximately 1:20,000. According to the cited references, this drug is “generally obtained over the counter in Latin America and is being used by Latinos for treatment of pain and/or fever.” (Moorman J. Dipyrone (metamizole) use in the United States: A lethal tango? 2006 Southern Med J 99:916 and Garcia S. et al. Metamizole use among Hispanics living in the United States: report if a survey conducted in a primary care setting in Miami. 2006 Southern Med J 99:924-926)

**Wednesday, May 20, 2015****Question:**

Atrazine is a herbicide used to control a variety of broadleafed weeds and grasses. Humans may be exposed to atrazine during manufacturing and formulating operations and during end-use applications such as farming and forestry. What is the the carcinogenic potential for this chemical?

**Answer:**

The cited reference evaluated epidemiologic evidence regarding the carcinogenic potential of atrazine. These investigators concluded: “A weight-of-evidence approach leads to the conclusion that there is no causal association between atrazine and cancer and that occasional positive results can be attributed to bias or chance. Atrazine appears to be a good candidate for a category of herbicides with a probable absence of cancer risk. Atrazine should be treated for regulatory and public health purposes as an agent unlikely to pose a cancer risk to humans.” (Boffetta P et al. Atrazine and cancer: a review of the epidemiologic evidence. 2013 Eur J Cancer Prevention 22(2): 169-180)

**Tuesday, May 19, 2015****Question:**

What is polymethylmethacrylate (PMMA) and what is its use in surgical practice?

**Answer:**

Bone cement, polymethylmethacrylate (PMMA), is the synthetic polymer of methyl methacrylate (MMA). It has been commercially used since the 1930's and its use in arthroplasty was popularized in the 1960's. Concerns have been raised regarding inhalational exposure to health care professionals for MMA during operative orthopedic procedures. However significant serum levels of MMA following inhalational exposure to humans have never been documented. (Homlar KC et al. Serum levels of methyl methacrylate following inhalational exposure to polymethylmethacrylate bone cement. 2013 J Arthroplasty 28:406-409)

**Monday, May 18, 2015****Question:**

A number of studies have reported an association between exposure to cooking oil fumes and which cancer?

**Answer:**

Some studies have shown an association (but not confirmed causation) between exposure to cooking oil fumes and the development of lung cancer. (Lee T and Gany F. Cooking oil fumes and lung cancer: A review of the literature in the context of the U.S. population. 2013 J Immigrant Minority Health 15:646-652)

**Friday, May 15, 2015**

**Question:**

Henna has been used as a ceremonial and decorative dye for skin hair and nails for centuries, “and as an expression of body art, especially in Islamic and Hindu cultures in the Arab, African and Indian world”. An extensive literature describing contact effects and systemic allergy related to henna exists. What is henna?

**Answer:**

The cited reference notes “Henna is the dried and powdered leaf of the dwarf evergreen shrub *Lawsonia inermis*, a member of the family *Lythraceae*. The henna plant thrives in arid climates. Saudi Arabia, Iran, Sri Lanka, India, Egypt and the Sudan are its major producers. When applied to the skin, hair, or nails, the pigment lawsone (2-hydroxy-1,4-naphthoquinone; CI 75480; Natural Orange 6), which is present at a concentration of < 2% in henna leaves and natural henna preparations, interacts with the keratin therein to give them a reddish-brown (‘rust-red’) colour; therefore, a frequently used synonym is ‘red henna’” (deGroot AC. Side effects of henna and semi-permanent ‘black henna’ tattoos: A full review. 2013 Contact Derm 69:1-25)

**Thursday, May 14, 2015**

**Question:**

Reports of divers and shell collectors being stung while handling cone snails have appeared in the medical as well as the lay literature. What are the toxins contained in cone snails and what are their mechanisms of action?

**Answer:**

The cited reference notes that contained in the various species that make up the superfamily Conoidea are a variety of so-called “conotoxins”. The authors go on to describe “The most extensively studied superfamilies are the A-, M- and O-superfamilies. Peptide families found within the A-super- family include the alpha-conotoxins and alpha A-conotoxins, both of which are competitive nicotinic acetylcholine receptor antagonists. In addition, there are kappa A-conotoxins which may act by blocking voltage-gated potassium channels. In the M-superfamily, most notable are the mu-conotoxins which block voltage-gated sodium channels. (McIntosh JM and Jones RM. Cone venom-from accidental stings to deliberate injection. 2001 Toxicol 39: 1447-1451)

**Wednesday, May 13, 2015**

**Question:**

What is the most important component of foundry dust and what disease is associated with exposure to this dust?

**Answer:**

According to the cited reference, the most important component of foundry dust is crystalline silica (quartz). This material comes from the sand that is used in cores and molds used in the process of pouring molten iron. The authors of the cited reference note “....a major respiratory health concern associated with foundry work is silicosis”. (Koskela K et al. Pulmonary inflammation in foundry workers. 2015 JOEM 57(2): 124-128)

**Tuesday, May 12, 2015**

**Question:**

Noise is considered by many to be an industrial “toxicant” exposure. What is the difference between so-called “impulse noise” and “continuous noise”?

**Answer:**

“Impulse noise” is characterized by “having a very high pressure level of very short duration” while “continuous noise” is noise that is “steady background noise from machinery” and is more typical of industrial settings. Impulse noise is typical of noise produced by the discharge of a firearm. (Nakashima A and Farinaccio R. Review of weapon noise measurement and damage risk criteria: Considerations for auditory protection and performance. 2015 Mil Med 180:401-408)

**Monday, May 11, 2015**

**Question:**

What are the most common industrial and non-industrial sources of exposure to the chemical acrylonitrile?

**Answer:**

The cited reference notes “Acrylonitrile is an important industrial chemical used in the manufacture of acrylic and modacrylic fibers, resins, plastics elastomers, adiponitrile and nitrile rubber for various consumer goods.” The authors go on to states that “Potential nonindustrial exposures arise from the burning of biomass (e.g. wildfires and fuel wood) and as a component of tobacco smoke.” (Marsh GM and Zimmerman SD. Mortality among chemical plant workers exposed to acrylonitrile. 2015 JOEM 57(2): 134-145)

**Friday, May 8, 2015**

**Question:**

Zolpidem is an imidazopyridine drug that is often used to treat insomnia. What are the so-called “complex behaviors” associated with the use of this drug?

**Answer:**

The cited reference notes that “The ingestion of zolpidem and other hypnotic sedative medications for the treatment of insomnia has been associated with sleepwalking and other complex behaviors including sleep eating and sleep driving.” (Poceta JS. Zolpidem ingestion, automatisms and sleep driving: A clinical and legal case series. 2011 J Clin Sleep Med 7(6): 632-638)

**Thursday, May 7, 2015**

**Question:**

What is the phenomenon known as “radiation recall”?

**Answer:**

The cited reference notes: “Radiation recall is an acute inflammatory reaction confined to previously irradiated areas that can be triggered when chemotherapy agents are administered after radiotherapy. It remains a poorly understood phenomenon, but increased awareness may aid early diagnosis and appropriate management. A diverse range of drugs used in the treatment of cancer has been associated with radiation recall.” (Burris HA and Hurtig J. Radiation recall with anticancer agents. 2010 The Oncologist, 15:1227–1237)

**Wednesday, May 6, 2015**

**Question:**

Some patients who suffer postoperative nausea and vomiting do not respond to ondansetron. Based on the relevant pharmacogenetics what is a likely mechanism for this phenomenon?

**Answer:**

The cited reference reports “One possible mechanism for this failure is ultrarapid drug metabolism via the cytochrome P-450 system, specifically the enzyme CYP2D6. Ultrarapid metabolism is seen in patients with multiple functional copies (3 or more) of the CYP2D6 allele.” (Candiotti KA et al. The impact of pharmacogenetics on postoperative nausea and vomiting. 2005 Anesthesiology 102:543-549)

**Tuesday, May 5, 2015**

**Question:**

How does the labeling of K2 and related “synthetic marijuana” protect the manufacturers of these substances from prosecution?

**Answer:**

These products are usually labeled “Not for human consumption”. The cited article notes: “This label has kept these products from being subjected to the Federal Analogue Act of 1986, which states “A controlled substance analogue shall, to the extent intended for human consumption, be treated, for the purposes of any Federal law as a controlled substance in schedule I”. (emphasis added) (United States, 1986). Consequently, in the absence of specific regulations of these substances, such as scheduling and bans, this labeling essentially transfers all responsibility for the user’s safety from the manufacturers and distributors to the consumer, who is often unaware of the product’s potential danger.” (Brents LK and Prather PL. The K2 spice phenomenon: emergence, identification, legislation, and metabolic characteristics if synthetic cannabinoids in herbal incense. 2014 Drug Metab Rev 46(1): 72-85)

**Monday, May 4, 2015**

**Question:**

The abuse of marijuana concentrates (e.g. “wax”, “butane honey oil” etc.) is increasing in the US. How are these concentrates abused and how does the levels of THC in leaf marijuana compare with levels of THC in marijuana concentrates? What has been the primary hazard noted in the manufacture and production of illicit marijuana concentrates?

**Answer:**

According to the DEA’s 2014 National Drug Threat Assessment Summary “These concentrates can be abused using e-cigarettes or consumed in edibles, and have significantly higher tetrahydrocannabinol (THC) levels than leaf marijuana. In 2013, the THC content of leaf marijuana averaged 12.55 percent, while the THC content of marijuana concentrates averaged 52 percent, with some samples testing over 80 percent.” The cited monograph goes on to note “Highly flammable butane gas is used to extract the THC from the marijuana leaf, and has resulted in explosions, injuries, and deaths.” (<http://www.dea.gov/resource-center/dir-ndta-unclass.pdf>, accessed March 2015)

**Friday, May 1, 2015**

**Question:**

The incidence of the neonatal abstinence syndrome in the USA has increased. What are the clinical manifestations of the so-called neonatal abstinence syndrome?

**Answer:**

According to the cited reference the neonatal abstinence syndrome “typically manifests in the first few days of life as hypertonia, autonomic instability, irritability, poor sucking reflex, impaired weight gain, and less commonly, seizures”. (Tolia V et al. Increasing incidence of the neonatal abstinence syndrome in U.S. neonatal ICUs. 2015 NEJM, published on April 26, 2015, at NEJM.org. DOI: 10.1056/NEJMsa1500439)

**Thursday, April 30, 2015**

**Question:**

What is endrin?

**Answer:**

Endrin is a solid, white, almost odorless substance that was used as a pesticide to control insects, rodents, and birds. Endrin has not been produced or sold for general use in the United States since 1986. (<http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=114>; accessed March 2015)

**Wednesday, April 29, 2015**

**Question:**

What is the mechanism for acute hepatotoxicity related to the industrial chemical carbon tetrachloride (CCl4)?

**Answer:**

The cited reference notes “The mechanisms of acute CCl4 hepatotoxicity involve immediate cleavage of CCl4 by CYP2E1 in hepatocytes, which generates the trichloromethyl radical, leading to lipid peroxidation and membrane damage. Subsequently, activated hepatic macrophages (Kupffer cells) produce toxic mediators (e.g., inflammatory cytokines, reactive oxygen intermediates, and eicosanoids), resulting in the injury of parenchymal cells.” (Wahlang B et al. Toxicant-associated steatohepatitis. 2013 Toxicol Path 41: 343-360)

**Tuesday, April 28, 2015**

**Question:**

The treatment of multiple myeloma in some patients has been improved by the addition of thalidomide (and its derivatives) to standard chemotherapy regimens. What serious complication has arisen as a result of adding thalidomide to the treatment protocols for multiple myeloma?

**Answer:**

Thalidomide has been associated with prothrombotic effects including the development of deep vein thrombosis. The cited reference reports “Combining thalidomide with chemotherapeutic agents or steroid preparations led to improved response rates in the treatment of multiple myeloma. However, deep vein thrombosis is one of the most serious side effects noted with this regimen, and how a thalidomide-based regimen causes DVT is unclear”. (Hoshi A et al. Activation of coagulation by a thalidomide-based regimen. 2011 Blood Coag & Fibrinolysis 22(6):532-540)

**Monday, April 27, 2015**

**Question:**

The tricyclic dibenzodiazepine clozapine is classified as an atypical antipsychotic. This drug is well known for its ability to induce agranulocytosis. What is the adverse cardiac effect associated with the drug clozapine?

**Answer:**

The adverse cardiac effect associated with clozapine is myocarditis. The cited reference reports: “Clozapine is uncommonly associated with myocarditis, which can be fatal. It typically occurs within the 1st month of treatment initiation, in young, previously healthy patients with cardiovascular history and normal baseline investigations. There are no known risk factors. Initial suspicion is frequently low: this condition is uncommon and it can present with a wide range of symptoms, some of which are remarkably nonspecific, and others, such as tachycardia, as expected early in the treatment and are benign. These factors may in fact lead to underestimating the prevalence of this condition.” (Munshi TA et al. Clozapine-induced myocarditis: Is mandatory monitoring warranted for its early recognition? Case Rep Psychiatry. 2014; 2014: 513108. Published online 2014 Jan 23. doi: 10.1155/2014/513108)

**Friday, April 24, 2015**

**Question:**

Some medications may be associated with corneal manifestations. Which commonly used drugs have been reported to cause corneal pathology and what are the mechanistic issues regarding this form of toxicity?

**Answer:**

The cited reference notes: “Systemic medications may reach the cornea via the tear film, aqueous humor, and limbal vasculature. The corneal changes are often the result of the underlying chemical properties of medications. Amphiphilic medications (amiodarone, chloroquine, suramin, clofazimine, etc.) may produce a drug-induced lipidosis and development of a vortex keratopathy. Antimetabolites (cytarabine) may lead to a degeneration of basal epithelial cells with formation of epithelial microcysts. Additionally, systemically administered medications and drug metabolites may lead to a stromal or endothelial deposition. Corneal changes may result in reduced visual acuity, photophobia, and ocular irritation, though these symptoms typically resolve following drug cessation. Corneal manifestations of systemic medications are often dose related, and may reflect the potential risk for lenticular or retinal changes.” (Hollander DA and Aldave AJ. Drug-induced corneal complications. 2004 Curr Opin Ophthalmol 15(6): 541-548)

**Thursday, April 23, 2015**

**Question:**

What was the substance known as “Mictal”?

**Answer:**

“Mictal” was the trade name for a weight loss “drug” marketed in the early 1980’s in the form of tablets containing dinitrophenol (DNP). DNP has been infamous in its association with a variety of adverse effects (including death) in individuals who have taken this chemical as a weight loss adjunct. Grundlingh J, et al. 2,4-dinitrophenol (DNP): a weight loss agent with significant acute toxicity and risk of death. 2011 Journal of Medical Toxicology, 7(3): 205-212.

**Wednesday, April 22, 2015**

**Question:**

Metalloproteinase enzymes are major components of most Crotalid and Viperid venoms. These enzymes are thought to be responsible for which effects associated with these venoms?

**Answer:**

The cited reference notes that snake venom metalloproteinases (SVMPs) are “notorious for their hemorrhagic activity”. In addition these authors point out other activities associated with these enzymes including fibrinogen-olytic, prothrombin activating, blood coagulation factor X activating, apoptotic, platelet aggregation inhibition, pro-inflammatory and inactivation of blood serine proteinase inhibitors. (Markland FS and Swenson S. Snake venom metalloproteinases. 2013 Toxicon 62:3-18)

**Tuesday, April 21, 2015**

**Question:**

What is the highest concentration of the topical insect repellent DEET (N, N-diethyl-m-toluamide) recommended for use in children by the American Academy of Pediatrics?

**Answer:**

The cited reference reports that “The American Academy of Pediatrics recommends use of formulations containing no more than 30% DEET in children.” (The Medical Letter, April 13, 2015, 57(1466):53)

**Monday, April 20, 2015**

**Question:**

New and highly effective drugs have recently been introduced for the treatment of hepatitis C. These drugs include Sovaldi (sofosbuvir) and Harvoni (sofosbuvir/ledipasvir). What serious effects have recently been reported with the use of these drugs in combination with amiodarone?

**Answer:**

The cited reference reports “The FDA recently announced changes in the labeling of the hepatitis C drugs Sovaldi and Harvoni to warn about a risk of serious and potentially fatal bradycardia when either drug is taken with the antiarrhythmic drug amiodarone.” (The Medical Letter, April 13, 2015, 57(1466): 58)

**Friday, April 17, 2015**

**Question:**

Antibiotic use is an important risk factor for the development of infection with *Clostridium difficile*. Which antibiotics are most often associated with the development of this infection?

**Answer:**

The cited reference notes “Ampicillin, amoxicillin, cephalosporins, clindamycin and fluoroquinolones are the antibiotics that are most frequently associated with the disease but almost all antibiotics have been associated with infection”. (Leffler DA and Lamont T. *Clostridium difficile* infection. 2015 NEJM372(16):1539-1548)

**Thursday, April 16, 2015**

**Question:**

What is the “ACE” Program?

**Answer:**

The ACE Program is the Assessment of Chemical Exposures (ACE) Program and it falls under the National Toxic Substances Incidents Program of the ATSDR. ACE provides training on how to perform an epidemiologic assessment after a chemical incident. The ACE Toolkit is a helpful resource to assist local authorities in responding to or preparing for a chemical release. The toolkit contains materials that can quickly be modified to meet the needs of a local team performing an epidemiologic assessment, including: Surveys; Consent forms; Medical chart abstraction form; Interviewer training manual; Epi Info™7 databases to enter and analyze the data.

When an incident occurs ACE provides technical assistance by forming a multi-disciplinary, often multi-agency, team to assist the state and local health department. Team members may assist from ATSDR headquarters in Atlanta, Georgia or deploy to the scene. Other support the ACE team can provide is: GIS mapping and assistance with sample methodologies; Clinical testing, if appropriate; Liaising with other federal agencies. (<http://www.atsdr.cdc.gov/ntsip/ace.html>; accessed February 2015)

**Wednesday, April 15, 2015**

**Question:**

What is the usual clinical course for healing of bite wounds from the brown recluse spider?

**Answer:**

According to the cited reference “The wound will typically heal within 3 weeks without permanent scarring; however, 20% will develop a necrotic ulcer that may remain symptomatic for months.” (Cacy J, Mold J. The clinical characteristics of brown recluse spider bites treated by family physicians. 1999 J Fam Prac 48:536-541 as cited in Delasota LA et al. Surgical treatment of a brown recluse spider bite: A case study and literature review. 2014 J Foot Ankle Surg 53:320-323)

**Tuesday, April 14, 2015**

**Question:**

Dronabinol (Marinol) is a pure synthetic oral form of delta-9-tetrahydrocannabinol (THC). What are the currently FDA approved uses for this drug?

**Answer:**

According to the cited reference, “Dronabinol is approved by the US Food and Drug Administration for the treatment of anorexia in AIDS and other wasting diseases and as an antiemetic agent in cancer patients undergoing chemotherapy”. (Milman G et al. Plasma cannabinoid concentrations during Dronabinol pharmacotherapy for Cannabis dependence. 2014 Ther Drug Monit 36:218-224)

**Monday, April 13, 2015**

**Question:**

What is the most common renal side effect of lithium therapy?

**Answer:**

According to the cited reference “Lithium is associated with increased risk of reduced urinary concentrating ability, hypothyroidism, hyperparathyroidism, and weight gain” however nephrogenic diabetes insipidus is the most common renal side effect associated with lithium therapy. (McKnight RF, et al. Lithium toxicity profile: a systematic review and meta-analysis. 2012 Lancet. 379(9817): 721)

**Friday, April 10, 2015**

**Question:**

What is the so-called palmar-plantar erythrodysesthesia syndrome (PPES)?

**Answer:**

Palmar-plantar erythrodysesthesia syndrome, also known as “hand-foot syndrome”, is a painful syndrome involving dermal toxicity with redness and tingling dysesthesias of the palms and soles progressing to painful swelling. The cited reference notes “The syndrome is associated with several chemotherapeutic agents, including methotrexate, mercaptopurine, cytarabine, fluorouracil, epirubicin, daunorubicin and doxorubicin. The occurrence of PPES appears to depend on peak drug level and total cumulative dose. In other words, it tends to be more common with bolus infusion than with continuous low-dose infusion, and in later cycles of chemotherapy than in the first cycle. However, not all patients experience this dose dependent phenomenon.” The mechanism for PPES is not known. (Hui YK and Cortes JE. Palmar-plantar erythrodysesthesia syndrome associated with liposomal daunorubicin. 2000 Pharmacotherapy 20(1):1221-1223)

**Thursday, April 9, 2015**

**Question:**

Can pseudoephedrine result in a false positive urine drug screen (immunoassay) for amphetamine?



**Answer:**

The cited reference states “The risk of false positive amphetamine immunoassay results from pseudoephedrine has been well established.” (DePriest AZ et al. Pseudoephedrine and false positive immunoassay urine drug tests for amphetamine. 2013 Pharmacotherapy 33(5):e88-e89)

**Wednesday, April 8, 2015****Question:**

What are the common drug interactions between oral emergency contraceptives and other drugs?

**Answer:**

According to the cited reference “No specific data are available regarding the interaction between oral emergency contraceptives and other drugs, but agents that can reduce the efficacy of other hormonal contraceptives may reasonably be assumed to affect the efficacy of emergency contraceptives in a similar way. In addition, because ulipristal is an antiprogesterin, it could interact with progestins in other contraceptives; therefore, if a woman who has taken ulipristal concurrently uses a contraceptive containing progestin, the efficacy of both the ulipristal and the other contraceptive could be reduced.” (Raymond EG and Cleland K. Emergency contraception. 2015 NEJM 372:1342-1348)

**Tuesday, April 7, 2015****Question:**

Indinavir sulfate (Crixivan) is a protease inhibitor that has been used to treat HIV patients and has been associated with the development of acute renal failure. What is the mechanism for the development of acute renal failure due to Indinavir?

**Answer:**

According to the cited reference, up to 28% of treated patients may develop “indinavir urolithiasis”. The authors point out “Indinavir may cause crystal formation within the renal tubules when urine pH is above 3.5. Crystallization in the urine may lead to intrarenal crystal deposition and [consequently] acute renal failure. (Kalaitzis C et al. Urological management of indinavir-associated acute renal failure in HIV-positive patients. 2007 Int Urol Nephrol 39:743-746)

**Monday, April 6, 2015****Question:**

The over-ingestion of black tea has been reported to be causative of acute renal failure. What is the basis for this potential association?

**Answer:**

According to the cited reference, “Black tea is a rich source of oxalate, containing 50-100 mg per mL”. These authors point out that more than 80% of tea consumed in the United States is black tea. They report a case of acute renal failure in an individual who consumed 16 cups of black tea daily and they posit that this excessive intake of black tea caused oxalate-induced acute renal failure in a 56-year-old male. (Syed F and Mena-Gutierrez A. A case of iced-tea nephropathy. 2015 NEJM 371(14): 1377-1378)

**Friday, April 3, 2015****Question:**

Methamphetamine can be synthesized from a variety of precursor chemicals. A primary interventional strategy to reduce the supply of methamphetamine includes the regulation of the various chemicals that may be used in the manufacture of methamphetamine. What are the most common precursor chemicals in the illicit production of methamphetamine?

**Answer:**

The most common precursor chemicals in the illicit manufacture of methamphetamine include ephedrine and pseudoephedrine as well as phenylpropanolamine (PPA) and phenyl-2-propanone (P2P or phenylacetone) (McKetin R. et al. A systematic review of methamphetamine precursor regulations. 2011 Addiction 106:1911-1924)

**Thursday, April 2, 2015****Question:**

Shiga toxin producing Escherichia coli (STEC) related hemolytic uremic syndrome is a serious cause of acute renal injury. What is the mechanism for Shiga toxin related kidney injury?

**Answer:**

The cited reference notes: “Shiga toxin causes combinations of thrombotic occlusion of glomerular and afferent arteriolar capillary lumens, glomerular cell swelling, apoptosis of glomerular and tubular cells acute tubular necrosis, and cortical necrosis.” (Spinale JM et al. Long term outcomes of Shiga toxin hemolytic uremic syndrome. 2013 Pediatr Nephro 28:2097-2105)

**Wednesday, April 1, 2015****Question:**

What is the clinical setting that lends itself to the development of methotrexate (MTX) related acute renal injury?

**Answer:**

The cited reference emphasizes: “Methotrexate is associated with dose dependent nephrotoxicity because the kidneys excrete 85-100% of the parent drug. At the conventional doses (approx. 20 mg/meter<sup>3</sup>) employed against rheumatologic diseases and most solid tumors, kidney function is not usually affected. In contrast, nephrotoxicity is generally seen following high-dose MTX (1000-3000 mg/meter<sup>3</sup>), which is reserved for treatment of aggressive malignancies, including osteosarcoma, breast cancer and acute lymphoblastic leukemia.” (Kumar N and Shirali AC. What is the best therapy for toxicity in the setting of methotrexate-associated acute kidney injury: High flux hemodialysis or carboxypeptidase G2? 2014 Semin Dial 27(3): 226-228)

**Tuesday, March 31, 2015****Question:**

What effects do the drugs acamprosate (Campral) and oral naltrexone have on “return to drinking” in adults who have suffered from alcohol use disorders?

**Answer:**

A recent systematic review and meta-analysis of the potential benefits and harms of acamprosate and oral naltrexone in adults with alcohol use disorders reported “Both acamprosate and oral naltrexone were associated with reduction in return to drinking. When directly compared with one another, no significant differences were found between acamprosate and naltrexone for controlling alcohol consumption. Factors such as dosing frequency, potential adverse events, and availability of treatments may guide medication choice.” (Jonas DE et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: A systematic review and meta-analysis. 2014 JAMA 311(18): 1889-1900)

**Monday, March 30, 2015****Question:**

The timber rattlesnake (*Crotalus horridus*) is a member of the pit viper family, whose habitat ranges widely from southwest Maine to northern Florida and west from southeast Minnesota to central Texas. What characterizes the envenomation from a timber rattlesnake?

**Answer:**

Envenomation from the timber rattlesnake is characterized by significant coagulopathy in conjunction with severe rhabdomyolysis. (Madey JJ et al. Facial diplegia, pharyngeal paralysis and ophthalmoplegia after a timber rattlesnake envenomation. 2013 *Pediatr Emerg Care* 29:1213-1216)

**Friday, March 27, 2015****Question:**

What structural changes reportedly occur in the brains of children who have been exposed to methamphetamine in utero?

**Answer:**

The findings reported in the cited study reveal “significant structural changes mainly of striatal, parietal and temporal areas” in children exposed prenatally to methamphetamine “compared to controls in 1) volumes, 2) cortical thickness and 3) group by gender interactions of volumes and cortical thickness.” The authors further state “Future prospective longitudinal studies are needed to address the precise trajectories of changes in brain volumes and cortical thickness over time, and their associated neuropsychological and neurodevelopmental impact.” (Roos A., et al. Structural brain changes in prenatal methamphetamine-exposed children. 2014 *Metab Brain Dis* 29:341-349)

**Thursday, March 26, 2015****Question:**

What are the specific patterns of increased maternal and fetal morbidity associated with methamphetamine use in pregnancy?

**Answer:**

A recent retrospective cohort study reported “After adjustment for multiple confounding variables on multivariable regression analysis, results indicated that compared with control subjects, methamphetamine users had greater odds of gestational hypertension (odds ratio [OR], 1.8; 95% confidence interval [CI], 1.6e 2.0), preeclampsia (OR, 2.7; 95% CI, 2.4e 3.0), intrauterine fetal death (OR, 5.1; 95% CI, 3.7e 7.2), and abortion (OR, 5.5; 95% CI, 4.9e 6.3). Additionally, these patients had higher odds of preterm birth (OR, 2.9; 95% CI, 2.7e 3.1), neonatal death (OR, 3.1; 95% CI, 2.3e 4.2), and infant death (OR, 2.5; 95% CI, 1.7e 3.7).” (Gorman MC et al. Outcomes in pregnancies complicated by methamphetamine use. 2014 *Am J Obstet Gynecol* 211(4): 429.e1-429.e7)

**Wednesday, March 25, 2015****Question:**

What is the HSDB database?

**Answer:**

HSDB is the Hazardous Substances Data Bank. It is a toxicology database that focuses on the toxicology of potentially hazardous chemicals. It provides information on human exposure, industrial hygiene, emergency handling procedures, environmental fate, regulatory requirements, nanomaterials, and related areas. The information in HSDB has been assessed by a Scientific Review Panel. The HSDB Scientific Review Panel meets several times yearly to review selected substances, add new records, and update records, as needed. (<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>; accessed March 2015)

**Tuesday, March 24, 2015****Question:**

A transdermal formulation of methylphenidate (Daytrana) is being used for the treatment of attention deficit hyperactivity disorder (ADHD). What is the effectiveness of this formulation when compared with oral long acting formulations of this drug? What is the duration of action of the transdermally delivered drug and what are the adverse effects that have been described associated with transdermal methylphenidate use?

**Answer:**

The cited reference reports that the transdermal formulation of methylphenidate is “probably as effective as oral long acting formulation of the drug.” The authors also state “The duration of action “for a 9-hour wear period is about 1.5 hours”. The authors of the cited reference go on to state that “Adverse effects such as anorexia, insomnia and tics have occurred more frequently with the patch formulation than with oral formulations, which may be related to the absence of first pass metabolism and mild skin reactions are common.” (The Medical Letter. March 16, 2015, 57(1464): 37-40)

**Monday, March 23, 2015****Question:**

What are the four groups of drugs that have been associated with the development of drug induced aseptic meningitis?

**Answer:**

The four groups of drugs that have been associated with the development of drug induced aseptic meningitis are nonsteroidal anti-inflammatory drugs (NSAIDs), antibiotics, immunosuppressive-immunomodulatory agents and antiepileptic drugs. (Moris G et al. The challenge of drug-induced aseptic meningitis. 1999 *Arch Int Med* 159(11): 1185-1194) as cited in Moris G and Garcia-Monco. The challenge of drug induced aseptic meningitis revisited. 2014 *JAMA Int Med* 174(9): 1511-1512)

**Friday, March 20, 2015**

**Question:**

What is the nature of most occupational exposures to the chemical boron?

**Answer:**

According to the cited reference "Occupational studies of workers exposed to dusts of sodium borates, the most important commercial forms of boron, have identified irritation of the respiratory tract and eyes, without measurable changes in pulmonary function. In an early cross-sectional surveillance of 629 U.S. workers in a sodium borate open-pit mining and production plant, past occurrence of symptoms of respiratory irritation such as dryness of the mouth, nose, or throat, dry cough, nose bleeds, and sore throat were reported at elevated frequencies in workers" (<http://www.atsdr.cdc.gov/toxprofiles/tp26-c3.pdf>; accessed February 2015)

**Thursday, March 19, 2015**

**Question:**

What are the current dosing recommendations for 20% intravenous lipid emulsion therapy per the American Society of Regional Anesthesia and Pain Medicine (ASRA)?

**Answer:**

The cited reference notes "The current intravenous lipid emulsion (ILE) administration guidelines are extrapolated from recommendations for LAST. Despite 7 years of history with ILE administrations, the recommendations are largely empiric without human trials to substantiate the optimal dose."

Current ASRA recommendations for dosing of 20% lipid emulsion are as follows:

1- Bolus 1.5 mL/kg (lean body mass) intravenously over 1 minute; 100 mL for a 70 kg patient; repeat bolus for persistent cardiovascular collapse.

2- Continuous infusion 0.25 mL/kg/min; 18 mL/min for a 70- kg patient; Can double the infusion rate for persistent hemodynamic instability; Continue infusion for at least ten minutes after hemodynamic recovery. (Neal JM et al. American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity. 2012 Reg Anesth Pain med 37:16-18 as cited in Cao D et al. Intravenous lipid emulsion in the emergency department: A systematic review of recent literature. 2015 J Emerg Med 48(3):387-397)

**Wednesday, March 18, 2015**

**Question:**

What is the clinical scenario known as LAST? What factors influence the development of LAST as well as its severity?

**Answer:**

"LAST" stands for "local anesthetic systemic toxicity". The cited reference notes "Factors known to influence the likelihood and severity of local anesthetic systemic toxicity (LAST) include individual patient risk factors, concurrent medications, location and technique of block, specific LA compound, total LA dose, timing of detection and adequacy of treatment." (Sagir A and Goyal R. An assessment of the awareness of local anesthetic systemic toxicity among multi-specialty postgraduate residents. 2014 Anesth. DOI 10.1007/s00540-014-1904-9)

**Tuesday, March 17, 2015**

**Question:**

Camphor is a toxicant well known for its adverse neurologic effects including altered mental status, seizures, coma and, in some cases, death. How is camphor metabolized?

**Answer:**

The cited reference notes "Camphor metabolism seems to follow first order kinetics. It has a half-life of approximately 15 hours and is initially metabolized via cytochrome P450-mediated reactions. Camphor is then oxidized by alcohol dehydrogenase in then liver and conjugated with glucuronic acid to become water-soluble for urinary excretion." (Santos CD and Cabot JC. Persistent effects after camphor ingestion: A case report and literature review. 2015 J Emerg Med 48(3): 298-304)

**Monday, March 16, 2015**

**Question:**

Which technique of heroin use is most likely to result in wound botulism and why?

**Answer:**

According to the cited reference the technique of so-called "skin popping" or "muscle popping" of heroin is most likely to result in the development of wound botulism. Heroin users engage in these practices because after long periods of use/abuse, their peripheral veins become sclerosed and no longer accessible. The authors note "This practice can result in formation of wounds and abscesses with anaerobic conditions, which can lead to germination of C. botulinum spores and subsequent production of toxin." (MacDonald E et al. Outbreak of wound botulism in people who inject drugs, Norway, October to November 2013. Euro Surveill. 2013; 18(45):pii=20630. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20630>)

**Friday, March 13, 2015**

**Question:**

Retail stores for the sale of marijuana have been established and are functioning in Colorado as well Washington state. Recently, voters in Alaska and Oregon have also approved retail marijuana sales What is the standard that Colorado has set for an edible serving of tetrahydrocannabinol (THC)?

**Answer:**

The cited reference notes that the state of Colorado has "set a standard size for an edible serving at no more than 10 mg of THC". (MacCoun RJ and Mello MM. Half-baked- The retail promotion of marijuana edibles. 2015 NEJM 372(11): 989-991)

**Thursday, March 12, 2015**

**Question:**

The FDA has recently approved a rapidly acting inhalable form of insulin called Afrezza. What are the most common adverse effects associated with this formulation?

**Answer:**

According to the cited reference "The most common adverse effects of Afrezza are throat pain or irritation, cough and hypoglycemia." The reference points out "In patients with type 2 diabetes, severe and non-severe hypoglycemia were more common in patients who took Afrezza (5.1% and 67% vs 1.7% and 30% with placebo). (The Medical Letter, March 2, 2015, 57(1463): 34-35)

**Wednesday, March 11, 2015**

**Question:**

What is the association between statin therapy and the development of pancreatitis?

**Answer:**

A recently published pooled analysis of randomized trial data reported use of statin therapy was “associated with a lower risk of pancreatitis in patients with normal or mildly elevated triglyceride levels”. (Preiss D et al. Lipid modifying therapies and risk of pancreatitis- am meta-analysis 2012 JAMA 308(8):804-811)

**Tuesday, March 10, 2015**

**Question:**

What is the FDA’s “FAERS” system?

**Answer:**

The FAERS system is the FDA Adverse Event Reporting System. This supports the FDA's post-marketing safety surveillance program for all approved drug and therapeutic biologic products. It contains adverse drug reaction reports FDA has received from manufacturers as required by regulation. (<http://www.fda.gov/Drugs/InformationOnDrugs/ucm135151.htm>; accessed February 2015)

**Monday, March 9, 2015**

**Question:**

Levamisole, an antihelminthic veterinary drug, contaminates a large percentage of the street cocaine used in the US today. How does the addition of levamisole to street cocaine enhance the psychoactive effects of cocaine?

**Answer:**

The cited reference notes: “Levamisole can enhance cocaine effects by conversion into the amphetamine-like drug aminorex.” Aminorex can be detected in urine up to 54 hours following the use of levamisole tainted cocaine. (Hess C et al. Metabolism of levamisole and kinetics of levamisole and aminorex in urine by means of LC-QTOF-HRMS and LC-QqQ-MS. 2013 Anal Bioanal Chem 405(12): 4077-4088)

**Friday, March 6, 2015**

**Question:**

What is the IPCS?

**Answer:**

The IPCS (International Program on Chemical Safety) is a joint activity of three cooperating international organizations: namely the United Nations Environment Programme (UNEP) , the International Labour Office (ILO) , and the World Health Organization (WHO) . The main objective of the IPCS is to carry out and disseminate evaluations of the hazards posed by chemicals to human health and the environment. (<http://www.cdc.gov/niosh/ipcs/ipccard.html>; accessed Feb 2015)

**Thursday, March 5, 2015**

**Question:**

What is the difference between DEA Schedule I and DEA Schedule II drugs?

**Answer:**

Schedule I drugs, substances, or chemicals are defined as drugs with no currently accepted medical use and a high potential for abuse. Schedule I drugs are the most dangerous drugs of all the drug schedules with potentially severe psychological or physical dependence. Some examples of Schedule I drugs are: heroin, lysergic acid diethylamide (LSD), marijuana (cannabis), 3,4-methylenedioxymethamphetamine (ecstasy), methaqualone, and peyote.

Schedule II drugs, substances, or chemicals are defined as drugs with a high potential for abuse, less abuse potential than Schedule I drugs, with use potentially leading to severe psychological or physical dependence. These drugs are also considered dangerous. Some examples of Schedule II drugs are: cocaine, methamphetamine, methadone, hydromorphone (Dilaudid), meperidine (Demerol), oxycodone (OxyContin), fentanyl, Dexedrine, Adderall, and Ritalin. (<http://www.dea.gov/druginfo/ds.shtml>; accessed December 2014)

**Wednesday, March 4, 2015**

**Question:**

In 1997, the National Heart, Lung and Blood Institute and the Dept. of Veterans Affairs organized and carried out the Digitalis Investigations Group (DIG) trial to evaluate the use of digoxin in heart failure patients. What were the primary findings of that study?

**Answer:**

The cited reference notes “In that trial, digoxin had no effect on the overall mortality in patients with heart failure but it reduced the rate of hospitalization both overall and for worsening heart failure.” (Ahmed A, et al. “Effects of digoxin at low serum concentrations on mortality and hospitalization in heart failure: a propensity-matched study of the DIG trial”. 2008 Int J Cardiol, 123:138–146 as cited in Kidambi S and Massad MG. “On van Gogh and the foxglove plant”. 2014 Cardiology, 127:164-166.

**Tuesday, March 3, 2015**

**Question:**

What is the so-called Agricultural Health Study (AHS)?

**Answer:**

According to the cited reference, The Agricultural Health Study (AHS) was “initiated in 1993 to study the potential health effects of agricultural pesticide exposures in commercial pesticide applicators, farmers, and their families in Iowa and North Carolina. The AHS is a collaborative research project including the U.S. National Cancer Institute, the U.S. National Institute of Environmental Health Sciences, and the U.S. Environmental Protection Agency (EPA).” A large number of articles have been published over the years with regard to this cohort. (Weichenthal S. et al. A review of pesticide exposure and cancer incidence in the Agricultural Health Study cohort. 2010 Env Health Perspect 118:1117-1125)

**Monday, March 2, 2015**

**Question:**

Long-term occupational exposure to formaldehyde has been suggested by some to be associated with an element of genotoxicity. Which biomarkers have been shown to be associated with formaldehyde related genotoxicity?

**Answer:**

The cited reference reports "A statistically significant association was found between formaldehyde exposure and biomarkers of genotoxicity, namely micronuclei (MN) in lymphocytes, nucleoplasmic bridges, nuclear buds and MN in buccal cells." (Ladeira C et al. Genotoxicity biomarkers in occupational exposure to formaldehyde-The case of histopathology laboratories. 2011 Mutation Res 721:15-20)

**Friday, February 27, 2015**

**Question:**

What is bisphenol A (BPA) and where is this substance found? Why are people concerned about BPA?

**Answer:**

Bisphenol A is a chemical widely used to make polycarbonate plastics and epoxy resins. Polycarbonate plastics have many applications including use in some food and drink packaging such as water and baby bottles, compact discs, impact-resistant used to coat metal products such as food cans, bottle tops, and water supply pipes. BPA can also be found in certain thermal paper products, including some cash register and ATM receipts. Some dental sealants and composites may also contribute to BPA exposure. One reason people may be concerned about BPA is because human exposure to BPA is widespread. The 2003-2004 National Health and Nutrition Examination Survey (NHANES), conducted by the Centers for Disease Control and Prevention (CDC), found detectable levels of BPA in 93% of Americans six years and older. Another reason for concern, especially for parents, may be because some laboratory animal studies report subtle developmental effects in fetuses and newborns exposed to low doses of BPA. ([http://www.niehs.nih.gov/health/assets/docs\\_a\\_e/bisphenol\\_a\\_bpa\\_508.pdf](http://www.niehs.nih.gov/health/assets/docs_a_e/bisphenol_a_bpa_508.pdf); accessed January 2015)

**Thursday, February 26, 2015**

**Question:**

What advice should be given to homeowners and renters who may have elevated levels of lead in their domestic drinking water?

**Answer:**

People should be advised as follows: "Flush your pipes before drinking, and only use cold water for consumption. The more time water has been sitting in your home's pipes, the more lead it may contain. Anytime the water in a particular faucet has not been used for six hours or longer, "flush" your cold-water pipes by running the water until it becomes as cold as it will get. This could take as little as five to thirty seconds if there has been recent heavy water use such as showering or toilet flushing. Otherwise, it could take two minutes or longer. Your water utility will inform you if longer flushing times are needed to respond to local conditions. Use only water from the cold-water tap for drinking, cooking, and especially for making baby formula. Hot water is likely to contain higher levels of lead. The two actions recommended above are very important to the health of your family. They will probably be effective in reducing lead levels because most of the lead in household water usually comes from the plumbing in your house, not from the local water supply." (<http://water.epa.gov/drink/contaminants/basicinformation/lead.cfm#How%20does%20lead%20get%20into%20my%20drinking%20water?>; accessed February 2015)

**Wednesday, February 25, 2015**

**Question:**

Liraglutide (Victoza) is a glucagon-like peptide-1 (GLP-1) agonist approved for the treatment of type 2 diabetes. What cancer risk has been warned about with regard to this drug?

**Answer:**

According to the cited reference "Thyroid C-cell hyperplasia has been reported with use of liraglutide in rats, and the FDA has required a box warning about the risk of thyroid C-cell tumors in the package insert." (The Medical Letter. February 16, 2015, 57(1462): 24-35)

**Tuesday, February 24, 2015**

**Question:**

During the first Gulf War some troops were treated with what compound as a prophylaxis against nerve agent toxicity?

**Answer:**

Some troops received the carbamate anticholinesterase compound pyridostigmine. (Abu-Qare AW and Abou-Donia MB. Sarin: health effects, metabolism and methods of analysis. 2002 Food and Cje, Tox 40:1327-1333)

**Monday, February 23, 2015**

**Question:**

What is a NIOSH "Health Hazard Evaluation" (HHE)? Who is permitted to request such an evaluation?

**Answer:**

An HHE is a study of a workplace. It is done to learn whether workers are exposed to hazardous materials or harmful conditions. In private sector and Federal workplaces an employee can request an HHE if he or she is currently an employee at the workplace of concern and has the signatures of two other employees. If the workplace has three or fewer employees, the signature of only one employee is enough. An officer of a labor union that represents employees for collective bargaining can request an HHE. Any management official may request an HHE on behalf of the employer. When the workplace is part of a State or local government, NIOSH authority is more limited than for the private and Federal sectors. The cooperation of the employer may be necessary before NIOSH can do an evaluation. (<http://www.cdc.gov/niosh/hhe/HHEprogram.html>; accessed January, 2015)

**Friday, February 20, 2015**

**Question:**

What are the bleeding risks associated with the use of SSRIs?

**Answer:**

The cited reference notes “Because they inhibit platelet aggregation, these agents (SSRIs) increase the risk of gastrointestinal bleeding; however, studies conflict on their association with brain hemorrhage.” In the cited study, these authors report on study results showing “Intracranial hemorrhage was related to SSRI exposure in both unadjusted (rate ratio [RR] 1.48, 95% confidence interval [CI] 1.22–1.78) and adjusted analyses (RR 1.51, 95% CI 1.26–1.81). Intracerebral hemorrhage was also associated with SSRI exposure in both unadjusted (RR 1.68, 95% CI 1.46–1.91) and adjusted (RR 1.42, 95% CI 1.23–1.65) analyses.” (Hackam DG and Mrkobrada M. Selective serotonin reuptake inhibitors and brain hemorrhage- a meta-analysis. 2012 Neurology 79:1862-1865)

**Thursday, February 19, 2015****Question:**

When NSAIDs are administered during the third trimester of pregnancy what adverse cardio-pulmonary effects might afflict the neonate?

**Answer:**

The cited reference reminds us that “Use of NSAIDs during the third trimester of pregnancy may cause premature closure of the ductus arteriosus and persistent pulmonary hypertension in the neonate.” The authors go on to state “these effects appear to be uncommon if the drug is discontinued 6-8 weeks before delivery”. (The Medical Letter. September 1, 2014, 56(1450): 81-82)

**Wednesday, February 18, 2015****Question:**

In 2012 drug manufacturers of statin medications were required by FDA to provide warnings regarding increases in blood glucose levels and hemoglobin A1C levels. What is the mechanism for the diabetogenic effect associated with statin medications?

**Answer:**

According to the cited reference “No mechanism for a diabetogenic effect of statins has been established. Some investigators have proposed that statins may cause an immune response that interferes with insulin signaling.” (The Medical Letter. September 1, 2014, 56(1450): 79-80)

**Tuesday, February 17, 2015****Question:**

What is the largest source for release of mercury into the environment on a worldwide basis?

**Answer:**

According to the cited reference “About 20% of the world's gold is produced by the artisanal and small-scale gold mining sector. This sector is also responsible for the largest releases of mercury to the environment of any sector globally. A major source of air pollution from mercury, artisanal and small-scale gold mining releases approximately 400 metric tons of airborne elemental mercury each year. Located in over 55 countries, small scale gold buying and refining facilities (commonly referred to as “Gold Shops”) are an important part of this production process, and are a major cause of air pollution from mercury. The burning of mercury-gold amalgam in these “Gold Shops” can have serious health effects both locally and globally.” (Accessed: February 2015)

**Monday, February 16, 2015****Question:**

Cisplatin (cis-diamminedichloroplatinum II) is a chemotherapeutic agent often used in the treatment of a variety of malignancies. What is the mechanism for the ototoxicity related to cisplatin therapy?

**Answer:**

The cited reference notes: “Histopathological studies of cisplatin ototoxicity indicate that damage to the outer hair cells progresses from the base to the apex of the cochlea and from the third to the first row of these cells, after which damage progresses to the inner hair cells.” The authors further indicate that “Damage is not limited to the hair cells – the supporting cells, stria vascularis and spiral ganglion are also affected.” They further point out “the stria vascularis of the cochlea is the region initially affected, leading to impaired uptake and secretion of potassium into the endolymph as well as impairment of the metabolic homeostasis of inner and outer hair cells, with resultant structural and functional damage.” (Goncalves MS et al. Mechanism of cisplatin ototoxicity: theoretical review. 2013 J Laryngology Otol 127:536-541)

**Friday, February 13, 2015****Question:**

How are the three different forms of chromium (Metallic, Chromium III compounds, and Chromium VI) classified with regard to carcinogenicity by IARC (International Agency for Research on Cancer)?

**Answer:**

Metallic chromium is classified by IARC as Group 3, Chromium (III) compounds are classified as Group 3 and Chromium VI is classified as Group 1. Group 1 chemicals are denoted by IARC as “carcinogenic to humans” and Group 3 chemicals are denoted by IARC as “not classifiable as to its carcinogenicity to humans”. (<http://www.atsdr.cdc.gov/toxprofiles/tp7-c8.pdf>; accessed January 2015)

**Thursday, February 12, 2015****Question:**

The mushroom *Pleurotus ostreatus* contains the toxin ostreolysin. What is the mechanism of toxicity for this toxin?

**Answer:**

The cited reference notes that ostreolysin is a 16-kDa acidic protein and is a member of the aegerolysin protein family. The authors note that the mechanism of toxicity for ostreolysin is “Transient increase in arterial blood pressure and then a progressive fall to mid-circulatory pressure accompanied by bradycardia, myocardial ischemia, and ventricular extrasystoles. The hyperkalemia resulting from the hemolytic activity probably plays an important role in its toxicity.” (Jo WS et al. Toxicological profiles of poisonous, edible, and medicinal mushrooms. 2014 Mycobiology 42(3):215-220)

**Wednesday, February 11, 2015****Question:**

Myopathy is a known toxicity associated with statin therapy. What is the incidence of severe myopathy in the form of rhabdomyolysis secondary to statin drugs?

**Answer:**

The cited reference points out that “the incidence of statin-induced myopathy is low...”. This article also notes “Data from the FDA adverse events reporting system (AERS) indicate a rhabdomyolysis incidence of 0.70 (95% CI: 0.62-0.79) per 100,000 patient-years.” (Law M and Rudnicka AR. Statin safety: a systematic review. 2006 Am. J. Cardiol. 97(8A), 52C-60C as cited in Harper CR et al. Clinical characterization and molecular mechanisms of statin myopathy. 2008 Expert review of cardiovascular therapy. 6(7): 955-969)

**Tuesday, February 10, 2015****Question:**

The terms “fry”, “wet” and “illy” are street names for what substance of abuse?

**Answer:**

“Fry”, “wet” and “illy” are street names for marijuana cigarettes tainted with formaldehyde or formaldehyde mixed with phencyclidine. (Gilbert CR et al. “Smoking wet” 2013 Tex Heart Inst J 40(1): 64-7)

**Monday, February 9, 2015****Question:**

Testing for cystic fibrosis (CF) involves measurement of sweat chloride levels. The focal point being that elevations of chloride in CF patients' sweat indicate dysfunction of the transmembrane conductance regulator (CFTR). Toxicity associated with which heavy metal has been suggested to also be associated with elevated sweat chloride levels?

**Answer:**

A recent study reported “elevated sweat chloride levels are found among persons exposed to arsenic in the absence of a genetic diagnosis of cystic fibrosis”. (Mazumdar M et al. Elevated sweat chloride levels due to arsenic toxicity. 2015 NEJM 371(6): 582-583)

**Friday, February 6, 2015****Question:**

What psychoactive substance is contained in the so called “San Pedro cactus” (Trichocereus pachanoi)?

**Answer:**

Mescaline is the psychoactive substance is contained in the so-called “San Pedro cactus” (Trichocereus pachanoi) (Bruhn JG et al. Ecstasy analogues found in cacti. 2008 Journal of Psychoactive Drugs, 40:2, 219-222)

**Thursday, February 5, 2015****Question:**

What is the National Toxicology Program (NTP)?

**Answer:**

The National Toxicology Program is an interagency program established in 1978 to coordinate toxicology research and testing across the Department of Health and Human Services. The program was also created to strengthen the science base in toxicology, develop and validate improved testing methods, and provide information about potentially toxic chemicals to health regulatory and research agencies, scientific and medical communities, and the public.

NTP is headquartered at the National Institute of Environmental Health Sciences (NIEHS). NIEHS is one of three core agencies that provide support for NTP activities. The other two agencies are:

The U.S. Food and Drug Administration, primarily through its National Center for Toxicological Research (NCTR/FDA); and  
National Institute for Occupational Safety and Health of the Centers for Disease Control and Prevention (NIOSH/CDC) (<http://ntp.niehs.nih.gov>; accessed January 2015)

**Wednesday, February 4, 2015****Question:**

What is the Clean Water Act?

**Answer:**

The Clean Water Act (CWA) establishes the basic structure for regulating discharges of pollutants into the waters of the United States and regulating quality standards for surface waters. The basis of the CWA was enacted in 1948 and was called the Federal Water Pollution Control Act, but the Act was significantly reorganized and expanded in 1972. "Clean Water Act" became the Act's common name with amendments in 1972.

Under the CWA, EPA has implemented pollution control programs such as setting wastewater standards for industry. We have also set water quality standards for all contaminants in surface waters. (<http://www2.epa.gov/laws-regulations/summary-clean-water-act>; accessed February 2015)

**Tuesday, February 3, 2015****Question:**

What chemical is also known as methanal, methylene oxide, oxymethylene, methylaldehyde, and oxomethane and is used in the production of fertilizer, paper, plywood, and urea-containing resins? This chemical is also used as a preservative in some foods?

**Answer:**

Formaldehyde is the chemical also known as methanal, methylene oxide, oxymethylene, methylaldehyde, and oxomethane. (<http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=39>; accessed January, 2015)

**Monday, February 2, 2015**



**Question:**

Etoposide is a chemotherapeutic agent sometimes used in cases of testicular cancer, small-cell lung cancer and non-Hodgkin's lymphoma. From what source is this drug derived and what is the mechanism of action for this drug?

**Answer:**

The cited reference notes that "etoposide is a semi-synthetic derivative of podophyllotoxin isolated from the dried roots and rhizomes of species of the genus Podophyllin". The authors also note that "Etoposide inhibits DNA topoisomerase II, thereby inhibiting DNA synthesis at the pre-mitotic stage." (Najar IA and Johri RK. Pharmaceutical and pharmacological approaches for bioavailability enhancement of etoposide. 2014 J Biosci 39(1): 139-144)

**Friday, January 30, 2015****Question:**

What percent of patients who suffer acetaminophen overdose will go on to develop renal failure?

**Answer:**

The cited reference notes that in the face of acetaminophen overdose renal failure is decidedly less common than hepatic injury and occurs in less than 1% of all patients. (Pakravan N et al. Renal injury at first presentation as a predictor for poor outcome in a severe paracetamol poisoning referred to a liver transplant unit. 2009 Eur J Clin Pharmacol 65:163-168)

**Thursday, January 29, 2015****Question:**

Antimony toxicity usually occurs as a result of occupational exposures or during treatment with drugs containing antimony. Antimony is used in the treatment of which disorders and what toxicities have been reported as a result of the therapeutic use of antimony compounds?

**Answer:**

The cited reference notes "As a therapeutic, antimony has been mostly used for the treatment of leishmaniasis and shistosomiasis. The major toxic side-effects of antimonials as a result of therapy are cardiotoxicity (~9% of patients) and pancreatitis, which is seen commonly in HIV and visceral leishmaniasis co-infections." (Sundar S and Chakravarty J. Antimony toxicity. 2010 Int J Env Res Public Health 7:4267-4277)

**Wednesday, January 28, 2015****Question:**

Unprotected, prolonged, occupational exposures to very high concentrations of vinyl chloride have been reportedly associated with the development of hepatic angiosarcoma in some workers. What is the posited latency period for the development of angiosarcoma of the liver that may be related to occupational vinyl chloride exposure?

**Answer:**

According to the cited literature reference the latency after first exposure may range from 24 to 56 years with a mean latency of 36.5 years. (Collins JJ et al. Surveillance for angiosarcoma of the liver among vinyl chloride workers. 2014 JOEM 56(11): 1207-1209)

**Tuesday, January 27, 2015****Question:**

Amyotrophic lateral sclerosis (ALS) is a rare degenerative motor neuron disease that is known to be progressive and irreversible. Is lead exposure a risk for the development of amyotrophic lateral sclerosis (ALS)?

**Answer:**

A recent meta-analysis reported "The risk of developing ALS among individuals with a history of exposures to lead was almost double (OR: 1.81; 95% CI, 1.39 to 2.36) on the basis of nine included case-control studies with specific lead exposure information, with no apparent heterogeneity across included studies. The attributable risk of ALS because of exposure to lead was estimated to be 5%." (Wang M, et al. A meta-analysis of observational studies of the association between chronic occupational exposure to lead and amyotrophic lateral sclerosis. 2014 JOEM 56(12): 1235-1242).

**Monday, January 26, 2015****Question:**

What is acetyl fentanyl, what are the effects on humans who might use this chemical and what are the legal issues surrounding this chemical?

**Answer:**

Acetyl fentanyl is (N-[1-phenethylpiperidin-4-yl]-N-phenylacetamide. The cited reference points out "Acetyl fentanyl is an opioid analgesic with no recognized medical uses. Studies suggest that it is 5 to 15 times more potent than heroin and has been associated with euphoria, altered mood, drowsiness miosis, cough suppression, constipation, and respiratory depression." The author goes on to point out that "What makes acetyl fentanyl potentially problematic is its legal status. It is not scheduled under the Controlled Substances Act but is considered an analogue of fentanyl. Thus acetyl fentanyl exists in a legal gray area: it is considered illicit if intended for human consumption but it evades regulation if packaged with the qualifier "not for human consumption". (Stogner JM. The potential threat of acetyl fentanyl: Legal issues, contaminated heroin and acetyl fentanyl "disguised" as other opioids. 2014 Ann Emerg Med 64(6): 637

**Friday, January 23, 2015****Question:**

The cited reference notes "E-cigarette liquids are typically solutions of propylene glycol, glycerol, or both, plus nicotine and flavorant chemicals. Which chemicals are produced as a result of the vaporization ("vapping") process associated with the use of e-cigarettes?

**Answer:**

The authors of the cited reference report they have "observed that formaldehyde-containing hemiacetals....can be formed during the e-cigarette "vapping" process. Formaldehyde is a known degradation product of propylene glycol that reacts with propylene glycol and glycerol during vaporization to produce hemiacetals." (Jensen RP et al. Hidden formaldehyde in e-cigarette aerosols. 2014 NEJM 372:392-394)

**Thursday, January 22, 2015**

**Question:**

Beta-blockers are known to be beneficial in patients with coronary artery disease however the use of these agents in COPD is controversial. What is the risk of COPD related mortality secondary to beta-blocker use?

**Answer:**

According to a recent systematic review, the pooled relative risk of COPD related mortality secondary to beta-blocker use was 0.69 (95% CI: 0.62-0.78. The authors of this study concluded "The results of this review are consistent with a protective effect of beta-blockers with respect to all cause mortality. Due to the observational nature of the included studies, the possibility of confounding that may have affected these results cannot be excluded. The hypothesis that beta-blocker therapy might be of benefit in COPD needs to be evaluated in randomized controlled trials." (Etminan M et al. Beta-blocker use and COPD mortality: a systematic review and meta-analysis. 2012 BMC Pulmonary Medicine 12:48)

**Wednesday, January 21, 2015**

**Question:**

The drug oritavancin (Orbactiv) is one of three lipoglycopeptide antibiotics currently available. Oritavancin is a long-acting drug administered via the IV route for acute bacterial skin and related infections due to gram positive bacteria in adults. What is the most serious potential adverse effect of this drug?

**Answer:**

The most serious potential adverse effect of the drug oritavancin involves serious hypersensitivity reactions that may be complicated by the prolonged half-life of this drug. The cited reference points out that "Patients with a history of a hypersensitivity reaction to another glycopeptide (e.g. vancomycin, teicoplanin, telavancin or dalbavancin) may be at increased risk." According to this reference, "Infusion-related reactions such as pruritis, urticaria, and flushing have also been reported." They go on to point out that "oritavancin, unlike telavancin, does not prolong the QT interval." (The Medical Letter, January 5, 2015, 57(1459):3-5.

**Tuesday, January 20, 2015**

**Question:**

What is the number one cause of lung cancer in people who have never smoked?

**Answer:**

Residential radon is the number one cause of lung cancer in people who have never smoked. According to the EPA, radon causes approximately 21,000 lung cancer deaths annually and about 10% of these are diagnosed in people who have never smoked. ( <http://www.epa.gov/radon/healthrisks.html>)

**Monday, January 19, 2015**

**Question:**

In patients with concomitant atrial fibrillation and congestive heart failure, a significant interaction between digoxin and amiodarone, in which amiodarone users, compared with nonusers, were at more risk of all-cause mortality has been identified. What is the basis for this effect?

**Answer:**

The cited reference notes: "Amiodarone may reduce digoxin renal clearance, decrease volume of distribution, and increase serum concentration, which could be the reason for the observed greater risk of all-cause mortality." (Gheorghade M et al. Contemporary use of digoxin in the management of cardiovascular disorders. 2006 Circulation 113:2556-2564) as cited in Shah M et al. Relation of digoxin use in atrial fibrillation and the risk of all-cause mortality in patients > 65 years of age with versus without heart failure." 2014 Am J Cardiol 114:401-406)

**Friday, January 16, 2015**

**Question:**

What is the NDC?

**Answer:**

The Drug Listing Act of 1972 requires registered drug establishments to provide the Food and Drug Administration (FDA) with a current list of all drugs manufactured, prepared, propagated, compounded, or processed by it for commercial distribution. (See Section 510 of the Federal Food, Drug, and Cosmetic Act (Act) (21 U.S.C. § 360)). Drug products are identified and reported using a unique, three-segment number, called the National Drug Code (NDC), which serves as a universal product identifier for drugs. FDA publishes the listed NDC numbers and the information submitted as part of the listing information in the NDC Directory which is updated daily. <http://www.fda.gov/Drugs/InformationOnDrugs/ucm142438.htm>; accessed January 2015)

**Thursday, January 15, 2015**

**Question:**

What ocular problems may result from occupational exposure to optical radiation in glassblowers?

**Answer:**

The cited reference notes, "The harmful effects of long term ocular exposure to cumulative levels of radiation in glassblowing have been recognized since the late 19th century. These effects include cataracts, pterygia, keratitis, and chronic dry eye problems." (Oriowo OM et al. Eye exposure to optical radiation in the glassblowing industry: An investigation in southern Ontario. 2000 Can J Pub Health 91(6): 471-474)

**Wednesday, January 14, 2015**

**Question:**

What is the effect of ketamine administration on intracranial and cerebral perfusion pressure?

**Answer:**

A recently published systematic review on this subject reported "None of the studies [analyzed] reported significant differences in cerebral perfusion pressure, neurologic outcomes, ICU length of stay or mortality." (Cohen L. et al. The effect of ketamine on intracranial and cerebral perfusion pressure and health outcomes: SA systematic review. 2014 Ann Emerg Med 65(1): 43-51)

**Tuesday, January 13, 2015**

**Question:**

The commonly produced isocyanates include toluene diisocyanate or methylbenzene diisocyanate (TDI) and methylene diphenyl diisocyanate or diphenyl-methane diisocyanate (MDI). What pathological process is responsible for the majority of adverse health effects attributed to this group of chemicals (i.e. isocyanates)?

**Answer:**

The cited article notes "Sensitization to isocyanates is the main reason for the increased burden of disease caused by these substances". The authors point out that "Sensitization is the process that occurs when exposure to a substance leads to an exaggerated response of the body at new exposure to that substance even at extremely low concentrations. In sensitization, the most pronounced reactions are exhibited in the airway system and the skin". (Verschoor L and Verschoor AH. 2014 Curr Opin Pulm Med 20:199-204)

**Monday, January 12, 2015**

**Question:**

What toxicity is related to ingestion of the perennial prairie forb known as blue wild indigo (false indigo) plant?

**Answer:**

The blue wild indigo plant is Baptisia australis. Ingestion of this plant is associated with nausea, vomiting, and diarrhea due to the toxin cytisine, a nicotinic acetylcholine receptor agonist. According to the cited reference, ingestion of Baptisia may also be associated with the development of vertigo, somnolence, tachypnea, cold sweats, dilated pupils, agitation and muscular contractions. (Anderson M et al. Baptisia poisoning: A new and toxic look-alike in the neighborhood. 2015 J Emerg Med 48(1):39-42)

**Friday, January 9, 2015**

**Question:**

What is 2,4 D?

**Answer:**

2,4 D is 2,4-Dichlorophenoxyacetic acid, an herbicide. With regard to the potential for adverse human health effects, the cited reference notes "Observations were made on 220 men exposed from 0.5 to 22 years of 2,4-D in a manufacturing plant. Medical evaluation revealed no difference when compared to a control group of 4600 men. In the exposed group 10 men were karyotyped. There was no effect on the structural integrity or arrangement of the genetic material of the lymphocyte chromosomes. In another study there were complaints of general weakness, rapid fatigue, frequent headache and vertigo among a number of workers at a plant manufacturing the amine salt and butyl ester. Cases of arterial hypotension were noted. There were possible indications of liver dysfunction which was noted in workers with long exposure to herbicides. In two groups of agricultural workers 250 and 45 respectively, excessive fatigue, Epigastric pains, anorexia and occasional respiratory tract symptoms and impaired taste sensitivity were reported. Reported cases of poisoning have been mainly the result of accidental or suicidal ingestion." (<http://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?/.temp/~Dn3GZu:1>; accessed December 2014)

**Thursday, January 8, 2015**

**Question:**

The lead hazard to individuals who practice recreational shooting on indoor ranges has been well documented over the years. What is the difference between the potential for lead exposure to individuals who fire on outdoor firing ranges versus those on indoor ranges?

**Answer:**

The cited reference reports: "There appears to be little difference in effect on blood lead from indoor or outdoor firing. This conclusion was enunciated earlier by Goldberg et al. for City of Los Angeles [small arms] instructors participating in uncovered outdoor ranges." (Goldberg RL, et al. Lead exposure at uncovered outdoor firing ranges. 1991 J Occup Med 33:718 -719 as noted in Gulson BL et al. Changes in blood lead of a recreational shooter. 2002 Sci Tot Env 293:143-150)

**Wednesday, January 7, 2015**

**Question:**

What is the epidemiology of death due to alcohol poisoning in the US?

**Answer:**

During 2010–2012, there was an annual average of 2,221 alcohol poisoning deaths, an age-adjusted rate of 8.8 deaths per 1 million population, among persons aged  $\geq 15$  years in the United States. Of these deaths, 1,681 (75.7%) were among adults aged 35–64 years, and 1,696 (76.4%) were among men. The highest death rate from alcohol poisoning was among men aged 45–54 years (25.6 deaths per 1 million). Although non-Hispanic whites accounted for the majority of alcohol poisoning deaths (67.5%; 1,500 deaths), the highest age-adjusted alcohol poisoning death rate was among American Indians/Alaska Natives (49.1 deaths per 1 million). A total annual average of 44 deaths (2.0%) involved persons aged 15–20 years, who were under the legal drinking age of 21. The age-adjusted alcohol poisoning death rate in states ranged from 5.3 per 1 million in Alabama to 46.5 per 1 million in Alaska. Twenty states had alcohol poisoning death rates greater than the overall national rate of 8.8 per 1 million, and two states (Alaska and New Mexico) had alcohol poisoning death rates  $>30$  per 1 million. States with the highest death rates were located mostly in the Great Plains and western United States, but also included two New England states (Rhode Island and Massachusetts). Alcohol dependence was listed as a contributing cause of death in an annual average of 677 (30.4%) of the deaths from alcohol poisoning, and hypothermia was listed as a contributing cause of death in an annual average of 134 (6.0%) deaths. Drug poisoning and drug use mental disorders were listed as contributing causes of death in an annual average of 62 (2.8%) and 86 (3.9%) deaths from alcohol poisoning, respectively. (MMWR. Alcohol poisoning deaths-United States, 2010-2012, January 6, 2015 63 (early release):1-5)

**Tuesday, January 6, 2015**

**Question:**

What potentially lethal electrolyte abnormality has been associated with the use of MDMA?

**Answer:**

Hyponatremia, at times severe and life threatening, has been associated with the use of MDMA. The mechanism for this is posited to involve dilutional effects of excessive water ingestion as well as the development of SIADH. (Hall AP and Henry JA. Acute toxic effects of "Ecstasy" (MDMA) and related compounds: overview of pathophysiology and clinical management. 2006 Br J Anaesthesia 96(6):678-685.

**Monday, January 5, 2015**

**Question:**

The puffer fish, also known as the globefish, fugu, or blowfish, is prized in many Asian cultures. Many species of this fish contain high levels of the toxin tetrodotoxin, a potentially deadly poison that is a heat-stable, acid-stable, non-protein, alkaloid toxin. Tetrodotoxin exerts its effects by blocking voltage-activated sodium channels, terminating nerve conduction and muscle action potentials, leading to progressive paralysis and, in extreme cases, to death from respiratory failure. Which form of puffer fish is currently permitted to be legally imported into the US?

**Answer:**

The cited reference notes “Only the frozen meat, skin, and male gonad from one species of puffer fish (*Takifugu rubripes*) from Japan, processed according to Japanese safety guidelines, is permitted to be imported into the United States a limited number of times per year, pursuant to an FDA/Japanese government agreement established in 1988. All other imported puffer fish products are prohibited.” (Cole JB et al. Tetrodotoxin poisoning outbreak from imported dried puffer fish-Minneapolis, Minnesota, 2014. *MMWR* January 2, 2015 63(51): 1222-1225)

**Friday, January 2, 2015****Question:**

What is the significance of yellow hyperplastic papules on the tongue of a patient who is being treated with hydroxychloroquine?

**Answer:**

Yellow hyperplastic papules on the tongue of a patient who is being treated with hydroxychloroquine is consistent with the diagnosis of exanthematous pustulosis. This problem can be treated with steroids and the lesions generally disappear after the drug is discontinued. (2015 NEJM Image challenge. January 1, 2015, <http://www.nejm.org> accessed January 2015)

**Thursday, January 1, 2015****Question:**

What are the so-called “greenhouse gases” and what activities are associated with the production of each?

**Answer:**

According to the EPA, the four main “greenhouse gases” are CARBON DIOXIDE (Carbon dioxide enters the atmosphere through burning fossil fuels, solid waste, trees and wood products, and also from certain chemical reactions (e.g., manufacture of cement)); METHANE (Methane is emitted during the production and transport of coal, natural gas, and oil. Methane emissions also result from livestock and other agricultural practices and by the decay of organic waste in municipal solid waste landfills.); NITROUS OXIDE (Nitrous oxide is emitted during agricultural and industrial activities, as well as during combustion of fossil fuels and solid waste.); FLOURINATED GASES (Hydrofluorocarbons, perfluorocarbons, and sulfur hexafluoride are synthetic, powerful greenhouse gases that are emitted from a variety of industrial processes). (<http://www.epa.gov/climatechange/ghgemissions/gases.html>; accessed December 2014)

**Wednesday, December 31, 2014****Question:**

VX (O-ethyl S-[2(diisopropyl-amino)ethyl] methylphosphonothioate) is a low volatility organophosphorus nerve agent. What is the most likely route for exposure following the nefarious release of this agent against human populations?

**Answer:**

The most likely route for exposure following the release of VX is via the dermal (skin) route. (Joosen MJA, et al. Timing of decontamination and treatment in case of percutaneous VX poisoning: A mini review. 2013 *Chemico-Biol Interactions* 203:149-153)

**Tuesday, December 30, 2014****Question:**

The risk for tetanus may be increased by a variety of conditions including burns, deep puncture wounds, crushing injuries, dental infections, animal bites, surgical abortions, pregnancy and the injection of illicit drugs. The risk is increased in any situation where necrotic tissue or foreign bodies predispose to growth of *Clostridium tetani*. The tetanus neurotoxin targets the neuromuscular junction. What are the primary determinates for the binding of tetanus neurotoxin at the neuromuscular junction?

**Answer:**

The cited reference reports that “the extracellular matrix proteins called nidogens (or entactins) appear to be the receptor for the tetanus neurotoxin to enter the neuromuscular junction.” (Bercsenyi K. et al: Tetanus toxin entry. Nidogens are therapeutic targets for the prevention of tetanus. 2014 *Science* 346: 1118-23).

**Monday, December 29, 2014****Question:**

What is tea tree oil and what has this substance been used for in complementary and alternative medicine practices? What are the potential toxicities of this oil?

**Answer:**

Tea tree oil (TTO) is a volatile essential oil derived from the Australian plant *Melaleuca alternifolia*. According to the cited reference “TTO is composed of terpene hydrocarbons, mainly monoterpenes, sesquiterpenes and their associated alcohols”. These authors go on to state that TTO is “Employed largely for its antimicrobial properties” and “as the active ingredient in many topical formulations used to treat cutaneous infections.” It is widely available over the counter world over. Topical exposure to TTO may result in irritant and/or allergic reactions. TTO can be harmful if ingested however no cases of human deaths have been reported. (Carson CF et al. *Melaleuca alternifolia* (Tea Tree) oil: A review of antimicrobial and other medicinal properties. 2006 *Clin Micro Rev.* 19(1): 50-62)

**Friday, December 26, 2014****Question:**

Aspirin is commonly used as an analgesic as well as a cardio-protective agent. What ocular problem has been posited to be associated with long-term use of low dose aspirin?

**Answer:**

Some authors have posited an association between the development of age related macular degeneration and long-term aspirin use. One recent longitudinal population based study of age related eye diseases reported “Among an adult cohort, aspirin use 5 years prior to observed incidence was not associated with incident early or late AMD. However, regular aspirin use 10 years prior was associated with a small but statistically significant increase in the risk of incident late and neovascular AMD”. (Klein B, et al. 2012 JAMA 308(23): 2469-2478)

**Thursday, December 25, 2014****Question:**

What chemical constituent of self-tanning products is usually responsible for the “bronzing effects” of these products?

**Answer:**

Dihydroxyacetone (DHA) is the chemical constituent of self-tanning products that is usually responsible for the “bronzing effects” of these products. DHA is a triose carbohydrate compound derived from the fermentation of glycerine and, according to the cited reference, was first recognized as a skin-coloring agent in the 1920's. (Bovenschen HJ et al. Contact dermatitis to self-tanning products. 2009 Contact Derm 60:290-291)

**Wednesday, December 24, 2014****Question:**

Tens of thousands of US workers may be exposed to asphalt fumes in the roofing, road building, paving and asphalt manufacturing industries. What biomarkers have been used as indicators of exposure to or effects of asphalt fumes?

**Answer:**

Urinary thioether excretion, glucaric acid metabolites in urine, detection of mutagens in urine, sister chromatid exchange and primary DNA damage in lymphocytes, urinary 1-hydroxypyrene, and DNA or protein adducts have been described as indicators of exposure to or effects of asphalt fumes. (NIOSH hazard Review. Health Effects of Occupational Exposure to Asphalt. 2000. <http://www.cdc.gov/niosh/docs/2001-110/pdfs/2001-110.pdf>; accessed November 2014)

**Tuesday, December 23, 2014****Question:**

What is ChemView?

**Answer:**

ChemView is a database established by the U.S. EPA. The ChemView database can be used to get information on chemical health and safety data received by EPA and EPA's assessments and regulatory actions for specific chemicals under the Toxic Substances Control Act (TSCA). ([www.epa.gov](http://www.epa.gov); accessed November 2014)

**Monday, December 22, 2014****Question:**

What is cytosine and what is its utility in assisting smoking cessation?

**Answer:**

Cytosine is a partial agonist at the nicotinic acetylcholine (alpha-4, beta-2) receptor that seems to mediate nicotine dependence. This substance is highly effective in assisting smoking cessation. The cited reference notes the use of cytosine “almost doubles the chances of quitting [smoking] at six months.” It has been noted that cytosine has been available for use as a modality to assist individuals to stop smoking in Eastern Europe for the past 50 years. (Walker N et al. Cytosine versus nicotine for smoking cessation. 2014b NEJM 371(25): 2353-2362)

**Friday, December 19, 2014****Question:**

What are kretek cigarettes?

**Answer:**

The cited reference notes “Kretek cigarettes contain clove buds in addition to tobacco in the filler (up to 40%) that gives them their unique taste and smell. In addition to the clove buds they also contain flavor ingredients according to the smoking preferences of the different consumer groups.” (Roemer E. et al. Toxicological assessment of kretek cigarettes Part 6: The impact of ingredients added to kretek cigarettes on smoke chemistry and in vitro toxicity. Regul. Toxicol. Pharmacol. (2014), <http://dx.doi.org/10.1016/j.yrtph.2014.11.016>)

**Thursday, December 18, 2014****Question:**

Clostridia species are spore-forming, anaerobic, gram positive bacilli commonly found in soil and marine sediments. Which specific clostridial species are responsible for producing botulinum toxins?

**Answer:**

Clostridium botulinum produces seven serologically distinct botulinum toxin types (A–G). Of these, human botulism is caused primarily by toxin types A, B, or E, and rarely by F. Several related clostridial species can produce botulinum toxins as well; toxin type E can be produced by C. butyricum and type F can be produced by C. baratii. ([http://www.cdc.gov/ncezid/dfwed/PDFs/bot-overview\\_508c.pdf](http://www.cdc.gov/ncezid/dfwed/PDFs/bot-overview_508c.pdf); accessed November, 2014)

**Wednesday, December 17, 2014****Question:**

The neuraminidase inhibitors oseltamivir (Tamiflu) and zanamivir (Relenza) are often used for therapy and chemoprophylaxis of influenza. The most commonly reported adverse effects of these drugs include headache, nausea and vomiting. What are the reported potential neuropsychiatric adverse effects associated with taking these drugs?

**Answer:**

According to the cited reference, “Neuropsychiatric events including self-injury and delirium have occurred in some patients taking neuraminidase inhibitors, particularly children treated with oseltamivir”. (The Medical Letter December 8, 2014,

**Tuesday, December 16, 2014****Question:**

What is the so-called Holiday Heart Syndrome (HHS) and what arrhythmias characterize this disorder?

**Answer:**

The cited reference notes “The term [HHS] was officially introduced in 1978 (by Ettinger et. al.) for describing the occurrence of an acute cardiac rhythm disturbance in apparently healthy people after an episode of heavy drinking, i.e., “binge drinking.” This disturbance disappeared with subsequent abstinence, leaving no residual heart disease. These occurrences had the particularity of being more frequent after weekends or holidays like Christmas or New Year’s Eve, which are known to be associated with increased alcohol ingestion, hence the name.” The authors further point out “HHS is mainly associated with supra ventricular arrhythmias, with AF being the most common cardiac arrhythmia in this syndrome. However, other less frequent types of arrhythmias can also occur, such as atrial flutter, paroxysmal atrial tachycardia, and isolated ventricular premature beats.” (Tonelo D et al. Holiday heart syndrome revisited after 34 years. 2013 Arq Bras Cardiol 101(2): 183-189)

**Monday, December 15, 2014****Question:**

Which congenital abnormalities may be associated with excessive intake of vitamin A during pregnancy?

**Answer:**

Excessive intake of vitamin A has been associated with cranio-facial abnormalities including cleft palate. (Ackermans M et al. Vitamin A and clefting: putative biological mechanisms. 2011 Nutrition Reviews 69(1):613-624

**Friday, December 12, 2014****Question:**

25I-NBOMe is a novel psychoactive substance that is a potent stimulant and serotonin receptor agonist. What are the clinical characteristics of toxicity related to this substance?

**Answer:**

The cited reference reports with regard to 25I-NBOMe toxicity, “Severe clinical features included seizures, aggression, self-harm and agitation, autonomic dysfunction, serotonin toxicity and rhabdomyolysis with acute renal failure. The most severe clinical features occurred after intravenous use.” (Hill SL, et al. Severe clinical toxicity associated with analytically confirmed recreational use of 25I-NBOMe: case series. 2013 Clin Tox 51(6): 487-492)

**Thursday, December 11, 2014****Question:**

Acrylonitrile is a colorless liquid chemical with a “sharp, onion or garlic-like odor. It is used in the manufacture of plastics, acrylic fibers and synthetic rubber. What is the potentially harmful metabolic breakdown product of acrylonitrile?

**Answer:**

Acrylonitrile is metabolized to cyanide (among other metabolites) and signs of cyanide toxicity have been reported in some cases following occupational exposure to this chemical. (Toxicological profile for acrylonitrile. 1990 ATSDR, <http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=78>; accessed December 2014)

**Wednesday, December 10, 2014****Question:**

The lipopeptide antibiotic drug daptomycin (Cubicin), often used to treat life threatening Gram positive hospital acquired infections, has been associated with the development of what potentially severe muscle disorder?

**Answer:**

According to the cited references, daptomycin has been associated with the development of clinically significant rhabdomyolysis. (Papadopoulos S et al. Rhabdomyolysis during therapy with daptomycin. 2006 Clin Inf Dis 42(12):e108-e110 as cited in Zimmerman JL and Shen MC. Rhabdomyolysis. 2013 Chest 144(3):1058-1065)

**Tuesday, December 9, 2014****Question:**

What are the primary ways lead contaminates drinking water?

**Answer:**

According to the EPA “The major sources of lead in drinking water are corrosion of household plumbing systems; and erosion of natural deposits. Lead enters the water (“leaches”) through contact with the plumbing. Lead leaches into water through corrosion – a dissolving or wearing away of metal caused by a chemical reaction between water and your plumbing. Lead can leach into water from pipes, solder, fixtures and faucets (brass), and fittings. The amount of lead in [drinking] water also depends on the types and amounts of minerals in the water, how long the water stays in the pipes, the amount of wear in the pipes, the water’s acidity and its temperature.” (<http://water.epa.gov/drink/contaminants/basicinformation/lead.cfm>; accessed October 2014)

**Monday, December 8, 2014****Question:**

What is the law known as "RCRA"?

**Answer:**

RCRA stands for the “Resource Conservation and Recovery Act”. RCRA was enacted by the U.S. Congress in 1976 to address the huge volumes of municipal and industrial solid waste generated nationwide. This Act provides broad guidelines for the establishment of a national waste management program. The Act also provides the Administrator of the EPA (or his or her designee) with the necessary authority to develop these broad standards into specific requirements for the regulated community. RCRA allows for wide ranging criminal prosecution of illegal acts and issues related to hazardous wastes that may endanger people, communities and the environment. (www.epa.gov; accessed August 2014)

**Friday, December 5, 2014****Question:**

What is the association between environmental (atmospheric) exposure to ozone and cardiovascular morbidity and mortality?

**Answer:**

The authors of the cited reference note “Taken as a whole, there is weak coherence between the recent epidemiological associations of cardiovascular mortality and morbidity and ozone exposure, and there are few controlled exposure studies that have attempted to provide biological plausibility and possible biological mechanisms that explain the association between ozone and acute mortality.” These authors reported on 23 healthy individuals exposed in a randomized crossover fashion to clean air and to 0.3-ppm ozone for 2 hours while intermittently exercising and reported Immediately after ozone exposure. They reported “a 98.9% increase in interleukin-8, a 21.4% decrease in plasminogen activator inhibitor-1, a 51.3% decrease in the high-frequency component of heart rate variability, and a 1.2% increase in QT duration. Changes in interleukin-1B and plasminogen activator inhibitor-1 were apparent 24 hours after exposure. In agreement with previous studies, [they] also observed ozone-induced drops in lung function and an increase in pulmonary inflammation.” (Devlin RB et al. Controlled exposure of healthy young volunteers to ozone causes cardiovascular effects. 2012 Circulation 126:104-111)

**Wednesday, December 3, 2014****Question:**

When do withdrawal symptoms referable to cessation of drinking alcohol begin and when do they peak?

**Answer:**

According to the cited reference “Because of the short action of ethanol (beverage alcohol), withdrawal symptoms usually begin within 8 hours after blood alcohol levels decrease, peak at about 72 hours, and are markedly reduced by day 5 through 7 of abstinence.” (Schuckit MA. Recognition and management of withdrawal delirium (delirium tremens). 2014 NEJM 371:2109-2113)

**Tuesday, December 2, 2014****Question:**

What were the three major component materials identified in the dust generated by the collapse of the World Trade Center Towers on September 11, 2001?

**Answer:**

The three major components component materials identified in the dust generated by the collapse of the World Trade Center Towers on September 11, 2001, were gypsum, concrete and man made fibers. (Lioy PJ and Georgopoulos P. The anatomy of the exposures that occurred around the World Trade Center site. 2006 Ann NY Acad Sci 1076:54-79)

**Monday, December 1, 2014****Question:**

What is the most likely cause for the cardiac arrhythmias and muscle weakness often associated with barium poisoning?

**Answer:**

According to the cited reference, “Barium is a potent, non-specific inhibitor of the potassium IRC current and affects all types of muscle at micromolar concentrations. Gastrointestinal symptoms frequently occur early in the course of barium poisoning. Hypokalemia resulting from an intracellular shift of potassium and the direct effect of barium at the potassium channels explain the cardiac arrhythmias and muscle weakness which commonly occur in barium poisoning.” (Bhoelan BS et al. Barium toxicity and the role of the potassium inward rectifier current. 2014 Clin Tox 52:584-593)

**Friday, November 28, 2014****Question:**

Nitrogen mustard agents have the potential to be used as chemical weapons however there are no records of such use to date. There are three nitrogen mustard agents of concern designated as HN-1, HN-2 and HN-3 and each has characteristic odors. What are the characteristic odors associated with each of these nitrogen mustard agents?

**Answer:**

The cited reference reports “HN-1 has a faint, fishy or musty odor. HN-2 has a soapy odor at low concentrations and a fruity odor at higher concentrations. HN-3 may smell like butter almond”. (www.atsdr.cdc.gov; accessed November of 2014)

**Thursday, November 27, 2014****Question:**

What is the eosinophilia-myalgia syndrome (EMS) and historically what was the association between EMS and the substance tryptophan?

**Answer:**

The authors of the cited reference note: In 1989, “This syndrome was initially reported in three patients found to be taking L-tryptophan (L-Trp) as a nutritional supplement. The hallmarks of the syndrome included weakness, oral ulcers, abdominal pain, skin rash, increased serum aldolase, leukocytosis, and most tellingly, a striking eosinophilia accompanying severe myalgias.” They further point out “Because of the strong association of EMS with the taking of L-Trp, the Food and Drug Administration (FDA) called for voluntary recall of L-Trp-containing products in the middle of November 1989. The rapid outbreak at the end of 1989 in the face of almost no previously reported L-Trp-caused perturbations suggested that a contaminant [as opposed to the tryptophan itself] might be the cause. Further detective work led to the finding that one manufacturer, Showa Denko of Tokyo, Japan, probably supplied the majority of the L-Trp associated with EMS. Eventually, chromatographic “fingerprints” of L-Trp samples obtained from the afflicted individuals corroborated the source of the contamination as being Showa Denko. The fact that a single source of tryptophan was responsible for the EMS epidemic provided further evidence that product contamination was the key factor.”

“An inquiry into the manufacturing practices of Showa Denko revealed certain changes and deficiencies in the manufacture of the EMS-implicated L-Trp. In the contaminated samples, a chromatographic peak that was designated as “peak E” was found in many of the samples. This peak was reported to be 1,1'-ethylidenebis(tryptophan), often referred to as EBT. EBT

induced pathologic alterations in muscle similar to those found in EMS.” (Das YT, et al. Safety of 5-hydroxy-L-tryptophan. 2004 Tox Letters 150(1): 111-122)

**Wednesday, November 26, 2014**

**Question:**

Latrodectism is the term used to designate the constellation of clinical effects caused from the bite of the black widow spider (*Latrodectus mactans*). What are these clinical effects?

**Answer:**

The authors of the cited study indicate that the constellation of clinical effects caused from the bite of the black widow spider include “pain, anxiety, agitation, autonomic dysfunction manifested by tachycardia, hypertension and diaphoresis.” (Dart RC et al. A randomized, double-blind, placebo controlled trial of a highly purified equine F(ab)2 antibody black widow spider antivenom. 2013 Ann Emerg Med 61(4): 458-467)

**Tuesday, November 25, 2014**

**Question:**

What is locust bean gum, what is it used for and what is the safety profile for this material when applied for its intended use?

**Answer:**

According to the cited reference locust bean gum (LBG) is “a galactomannan polysaccharide (from the endosperm seed of the locust/carob tree (*Ceratonia siliqua* (L.) Taub) of the plant family of Leguminosae.) used as thickener in infant formulas with the therapeutic aim to treat uncomplicated gastroesophageal reflux”. The cited reference provides an integrated review of relevant toxicological databases as well as clinical evidence. The authors have determined that LBG was “not associated with any adverse toxic or nutritional effects in healthy term infants, while there are limited case-reports of possible adverse effects in preterms receiving the thickener inappropriately. Altogether, it can be concluded that LBG is safe for its intended therapeutic use in term-born infants to treat uncomplicated regurgitation from birth onwards.” (Meunier L et al. Locust bean gum safety in neonates and young infants. 2014 70(1):155-169)

**Monday, November 24, 2014**

**Question:**

What is the risk for adverse cardiovascular events in men who receive testosterone replacement therapy?

**Answer:**

The risk for adverse cardiovascular events in men who receive testosterone replacement therapy remains controversial. The author of the cited reference reports “Although recent reports raise the possibility of an increase in cardiovascular risk associated with testosterone-replacement therapy, other data do not show this risk, and the Endocrine Society suggests that a large scale, controlled study is needed to resolve the controversy.” (The Endocrine Society. The risk of cardiovascular events in men receiving testosterone therapy: an Endocrine Society statement. February 7, 2014 (<https://www.endocrine.org/~media/endosociety/Files/Advocacy%20and%20Outreach/Position%20Statements/Other%20Statements/The%20Risk%20of%20Cardiovascular%20Events%20in%20Men%20Receiving%20Testosterone%20Therapy.pdf>), as cited in Swerdloff R. testosterone replacement therapy. 2014 NEJM 371:2023-2034)

**Friday, November 21, 2014**

**Question:**

Trinitrotoluene (TNT) is widely used in the munitions industry. What is the primary health problem of concern for workers in this industry and what is the mechanism for this effect? Which exposure route is of special concern for TNT production workers?

**Answer:**

Considered an “Occupational Sentinel Health Event”, the development of anemia in the primary health problem in workers who work with and around TNT. The authors of the cited study indicate “there is evidence that TNT suppresses delta-aminolevulinic acid synthase, caused hemolytic anemia when methemoglobin is produced and causes oxidative damage to red blood cells.” Dermal absorption is of special concern with regard to TNT. (Mallon TM et al. Investigation of an outbreak of anemia cases at an Army trinitrotoluene munitions production plant from 2004 to 2005 and subsequent surveillance 2005-2013. 2014 Mil Med 179(11):1374-1383)

**Thursday, November 20, 2014**

**Question:**

What are the usual industrial uses for the chemical diborane and how does this chemical react in moist air at room temperature?

**Answer:**

Diborane is a colorless gas at room temperature with a repulsive, sweet odor. It mixes well with air and easily forms explosive mixtures. Diborane will ignite spontaneously in moist air at room temperature. Diborane is used in rocket propellants, as a reducing agent, as a rubber vulcanizer, as a catalyst for hydrocarbon polymerization, as a flame-speed accelerator, and as a doping agent. It is also used in electronics to impart electrical properties in pure crystals. ( [www.atsdr.gov](http://www.atsdr.gov); accessed October 2014)

**Wednesday, November 19, 2014**

**Question:**

What are so-called “landfill gases”? How are these gases produced? What are the typical constituents of landfill gases?

**Answer:**

Landfill gases are, quite simply, gases that are produced within, and emanate from, man made landfills. Landfill gases are typically composed of methane, carbon dioxide, nitrogen, oxygen, ammonia, NMOs (non-methane organic compounds), sulfides, hydrogen and carbon monoxide. These gases are produced via three basic processes: bacterial decomposition, volatilization and chemical reactions. (Landfill gas primer: An overview for environmental health professionals. Published by ATSDR November, 2001)

**Tuesday, November 18, 2014**

**Question:**

Arc welding produces ultraviolet radiation (UVR). Occupational exposure to this welding- associated UVR has been shown to increase the risk for which rare form of cancer?



**Answer:**

The cited reference notes that occupational welding increases the risk for the development of ocular melanoma. (Dixon AJ and Dixon BF. Ultraviolet radiation from welding and possible risk of skin and ocular malignancy. 2004 Med J Australia 181(3): 155-157)

**Monday, November 17, 2014****Question:**

Ingestion of what toxicant has been associated with the development of so-called "boiled lobster" skin rash followed by extensive desquamation within 48 hours?

**Answer:**

Ingestion of boric acid has been associated with a "boiled lobster" rash followed by extensive desquamation. (Lung D and Clancy C. "Boiled lobster" rash of acute boric acid toxicity. 2009 Clin Tox 47: 432)

**Friday, November 14, 2014****Question:**

Case reports have appeared in the medical literature describing a pink colored sediment in the urine of patients who have recently received propofol anesthesia. What is the proposed mechanism for the formation of pink urine associated with propofol anesthesia?

**Answer:**

The cited reference notes "pink urine syndrome" is "a rare condition described after surgery and propofol anesthesia." The authors go on to describe that "uric acid excretion in urine is increased by propofol and by V1 receptor stimulation associated with postoperative inappropriate antidiuretic hormone secretion. Low urinary pH decreases uric acid solubility, promoting the formation of amorphous uric acid crystals, which exhibit a characteristic pink color. Increasing the urinary pH dissolves the crystals thereby restoring normal urine color." The condition is noted to be benign. (Potton L et al. Pink urine. 2013 Intensive Care Med 39:389-390)

**Thursday, November 13, 2014****Question:**

Some have advocated for the use of low dose aspirin as a potential modality to prevent pregnancy loss. What is the effect of low dose aspirin given pre-conception on pregnancy outcome?

**Answer:**

In a multi-center study of over 1200 women, the cited reference concluded "Preconception-initiated low-dose aspirin was not significantly associated with livebirth or pregnancy loss in women with one to two previous losses. However, higher livebirth rates were seen in women with a single documented loss at less than 20 weeks' gestation during the previous year. Low-dose aspirin is not recommended for the prevention of pregnancy loss." (Schisterman EF et al. Preconception low-dose aspirin and pregnancy outcomes: results from the EAGeR randomised trial. 2014 Lancet 384(9937): 29-36)

**Wednesday, November 12, 2014****Question:**

The two types of heparin-induced thrombocytopenia have been identified. What are these and how are they characterized?

**Answer:**

There are two types of heparin-induced thrombocytopenia (HIT) and they are known as, Type I and Type II. According to the cited reference "Type I is the most common form of thrombocytopenia and is self-limiting. Mild thrombocytopenia occurs in the first 2 days after heparin initiation and normalizes even with continued heparin therapy. The mechanism of the thrombocytopenia is not autoimmune and is due to a direct effect of heparin on platelet activation." The author describes type II HIT as "A more serious form [and is] an immune mediated disorder characterized by the formation of antibodies against heparin-PF4 complex. This disorder has also been called heparin-associated immune thrombocytopenia (ITP), heparin-associated thrombocytopenia and thrombosis (HITT), and the white clot syndrome. (Lovecchio F. Heparin-induced thrombocytopenia 2014 Clin Tox 52(6): 579-583)

**Tuesday, November 11, 2014****Question:**

Fluoropolymers are fluorocarbon-based polymers containing strong carbon-fluorine bonds. These compounds are used in many products including water repellants, lubricants and sealants. Inhalational exposure to these compounds has been associated with the development of so called "fluoropolymer associated illness". The pathophysiology of this disorder remains somewhat controversial. What are the clinical characteristics that have been reportedly associated with "fluoropolymer associated illness"?

**Answer:**

According to the authors of the cited reference, fluoropolymer- containing products "have been associated with sporadic outbreaks of respiratory disease, sometimes severe, consisting of cough, shortness of breath and chest pain and occasionally leading to hospitalization, respiratory failure, acute respiratory distress syndrome and death." (Hays HL and Spiller H. Fluoropolymer-associated illness. 2014 Clin Tox 52:848-855)

**Monday, November 10, 2014****Question:**

What is the so-called HAZWOPER standard and which government agency developed and promulgates this standard?

**Answer:**

The HAZWOPER standard is the "Hazardous Waste Operations and Emergency Response" standard and can be found in its entirety in the Federal Register at 29 CFR 1910.120. HAZWOPER requires that workers be trained to perform their anticipated job duties without endangering themselves or others. (www.osha.gov; accessed September 2014)

**Friday, November 7, 2014****Question:**

What effect do proton pump inhibitors (PPIs) have on the drug clopidogrel?

**Answer:**

The cited reference points out that the CYP2C19 isoform converts clopidogrel to its active form. PPIs are known to inhibit CYP2C19 and thus can interfere with the activation of clopidogrel. This is especially true of the PPI drugs omeprazole and esomeprazole. The cited reference recommends patients taking clopidogrel who may require PPIs should take pantoprazole, lansoprazole or dexlansoprazole instead of omeprazole and esomeprazole. (The Medical Letter, October 27, 2014, 56(1454): 103-108)

**Thursday, November 6, 2014**

**Question:**

Pinpoint pupils unresponsive to naloxone have been reported in association with overdose of which antipsychotic drugs? What is the proposed mechanism for this phenomenon?

**Answer:**

Pinpoint pupils unresponsive to naloxone have been reported in association with overdose of ziprasidone and olanzapine. The authors of the cited reference note: "Pupil size is maintained by a balance between sympathetic and parasympathetic neurohumeral tones. We propose that an overdose of an alpha-1 receptor blocking agent, such as ziprasidone, or many of the other atypical antipsychotic agents results in unopposed parasympathetic stimulation. The clinical result is miosis." (Fasano CF et al. Pediatric ziprasidone overdose. 2009 Pediatr Emer Care 25(4): 258-259)

**Wednesday, November 5, 2014**

**Question:**

What are the principle adverse health effects associated with occupational exposure to asphalt and asphalt fumes?

**Answer:**

According to the National Institute for Occupational Safety and Health (NIOSH), the principle adverse health effects associated with acute occupational exposure to asphalt and asphalt fumes are irritation of the serous membranes of the conjunctivae and mucous membranes of the respiratory tract. Current research discusses possible associations between occupational exposures to asphalt and asphalt fumes and a variety of cancers including lung cancer however these associations remain controversial. (Hazard Review: Health Effects of Occupational Exposure to Asphalt, 2000 DHHS (NIOSH) Publication No. 2001-110)

**Tuesday, November 4, 2014**

**Question:**

While most patients suffering from acetaminophen (APAP) toxicity are managed using antidotal therapy with N-acetylcysteine, hemodialysis (HD) may be added to treat some seriously ill patients following massive APAP overdose. What effect does the application of HD to treat these patients have on the efficacy of co-administered N-acetylcysteine?

**Answer:**

The cited reference reports on a study of three (3) seriously ill patients suffering massive APAP overdose. These investigators found "hemodialysis more than doubles the clearance of both acetaminophen and acetylcysteine". They report "Extraction ratios of acetylcysteine across the dialysis circuit ranged from 73% to 87%". As a consequence, these authors "recommend doubling the dose [of acetylcysteine] during hemodialysis, with an additional half-load when dialysis exceeds 6 hours." (Silvotti M. et al. Antidote removal during haemodialysis for massive acetaminophen overdose. 2013 Clin Tox 51(9): 855-863)

**Monday, November 3, 2014**

**Question:**

What is CERCLA?

**Answer:**

CERCLA is the Comprehensive Environmental Response, Compensation and Liability Act of 1980 also known as "Superfund", was enacted to address abandoned hazardous waste sites in the U.S. The law has subsequently been amended, by the Superfund Amendments and Reauthorization Act of 1986 (SARA), and the Small Business Liability Relief and Brownfields Revitalization Act of 2002. (<http://www2.epa.gov/regulatory-information-topic/land-and-cleanup#rcra>; accessed October 2014)

**Friday, October 31, 2014**

**Question:**

What are the current FDA recommendations for the disposal of expired, unwanted or unused oxycodone and/or transdermal fentanyl and what is the stated rationale for this form of disposal for these drugs?

**Answer:**

According to the FDA, "There is a small number of medicines (including oxycodone and transdermal fentanyl) that may be especially harmful and, in some cases, fatal with just one dose if they are used by someone other than the person for whom the medicine was prescribed. To prevent accidental ingestion by children, pets, or anyone else, a few medicines have specific disposal instructions indicating they should be flushed down the sink or toilet as soon as they are no longer needed, and when they cannot be disposed of through a medicine take-back program." A list of the medications for which FDA specifically recommends disposal in this manner is available on the FDA website. (<http://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/ensuringsafeuseofmedicine/safedisposalofmedicines/ucm186187.htm#MEDICINES>; accessed September 2014)

**Thursday, October 30, 2014**

**Question:**

What percent of patients poisoned with carbon monoxide (CO) will manifest MRI evidence of basal ganglia lesions within 6 months of exposure?

**Answer:**

The cited study notes that the literature quotes an extremely wide variation of incidence for basal ganglia lesions with reported incidences ranging from 4% to 88%. However these authors studied 73 CO poisoned patients who underwent MR scanning on day 1, 2 weeks and 6 months post exposure. They report only one patient from this cohort manifesting globus pallidus lesions and they concluded "Basal ganglia lesions, including lesions of the globus pallidus, may be less common than previously reported." (Hopkins R O et al. Basal ganglia lesions following carbon monoxide poisoning. 2006 Brain Injury 20(3): 273-281)

**Wednesday, October 29, 2014**

**Question:**

Malaria continues to be a serious concern with regard to global health and malaria in pregnancy is responsible for approximately 15% of all maternal deaths in malaria endemic areas. What is the safety of the anti-malarial drug mefloquine in pregnancy?

**Answer:**

The use of the anti-malarial drug, mefloquine, has been controversial in pregnancy. However a recent systematic review reports looking at eighteen articles and found “no indications that mefloquine use during pregnancy carries an increased risk for the developing fetus”. (Gonzalez R et al. Mefloquine safety and tolerability in pregnancy: a systematic literature review. 2014 Malaria Journal 13:75-85)

**Tuesday, October 28, 2014****Question:**

What are the most likely predictive risk factors for the development of delayed neuropsychological sequelae following exposure to carbon monoxide?

**Answer:**

One study reported multivariate analysis revealing the Glasgow Coma Scale less than 9 and leukocytosis were independent prognostic factors for the development of delayed neuropsychological sequelae following exposure to carbon monoxide. The same study reported no significant correlation with age, gender, voluntary exposure, headache, transient loss of consciousness, GCS between 14 and 9, arterial lactate and carboxyhemoglobin concentration. Nonetheless, the predictive risk factors for the development of delayed neuropsychological sequelae following exposure to carbon monoxide remain somewhat controversial. (Pepe G et al. Delayed neuropsychological sequelae after carbon monoxide poisoning: predictive risk factors in the emergency department. A retrospective study. 2011 Scan J Trauma Resuscitation and Emerg Med 19:16-23)

**Monday, October 27, 2014****Question:**

During which months are brown recluse spider envenomations most prevalent?

**Answer:**

According to the cited reference, "A significant seasonal correlation was recently shown for brown recluse spider activity. For patients with suspected brown recluse spider bites (BRSB), we have observed seasonality. Among 45 cases with features consistent with a BRSB, 43 (95.6%) occurred during April–October. (Rader RK et al. Seasonality of brown recluse populations is reflected by numbers of brown recluse envenomations. 2012 Toxicol 60(1):1-3)

**Friday, October 24, 2014****Question:**

What health concerns regarding the use of so-called “Chinese dry wall” emerged during the year 2008?

**Answer:**

According to the cited reference “The health concerns involved possible health implications from exposure to sulfur gases emitted from Chinese-manufactured drywall. According to ATSDR based on the limited number of drywall samples tested, exposures to the estimated levels of hydrogen sulfide and sulfur dioxide from drywall samples manufactured in China between 2005 and 2006 were a public health concern. Short-term exposures might result in effects seen in both clinical and human epidemiologic studies. These include exacerbation of pre-existing respiratory conditions, eye and nasal irritation, headache, changes in vision, and weakness. Although less certain, longer term exposures may have increased the risk of damage to nasal tissue. Exposure to the estimated contaminant concentrations could diminish a resident’s quality of life by triggering irritant (eye, nose, and throat) and physical (respiratory, gastrointestinal) symptoms, leading to negative mood states, and altering daily activities.” ([http://www.atsdr.cdc.gov/drywall/docs/Drywall\\_HC\\_05-02-2014\\_508.pdf](http://www.atsdr.cdc.gov/drywall/docs/Drywall_HC_05-02-2014_508.pdf), accessed September 2014)

**Thursday, October 23, 2014****Question:**

Imatinib mesylate (Gleevec) is a kinase inhibitor widely used for a variety of leukemias and other malignancies. One of the reported adverse consequences associated with the use of this drug is the so-called “tumor lysis syndrome” (TLS). What is the tumor lysis syndrome?

**Answer:**

The cited reference notes “TLS occurs when the cellular components of tumor cells are released into the blood after lysis, typically after chemotherapy or radiation therapy. It is characterized by hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia, factors which may overtax the body’s homeostatic mechanisms and overwhelm the capacity for normal excretion of these materials. This, in turn, causes various manifestations of TLS, including acute renal failure and cardiac arrest due to electrolyte abnormalities. Malignancies, which typically result in TLS, are ones that possess a high proliferation rate and/or a large tumor burden, such as lymphomas and acute leukemias.” (McBride A and Westervelt P. Recognizing and managing the expanded risk of tumor lysis syndrome in hematologic and solid malignancies. 2012 J Hematol Onc 5(75):

**Wednesday, October 22, 2014****Question:**

All products containing hydrocodone have recently been re-classified by DEA as schedule II drugs (previously they were listed as schedule III). The reference cited below notes that schedule II drugs are “those that have an accepted medical use in the US and a high potential for abuse that can result in severe psychological and physical dependence.” What are the effects of this re-scheduling of hydrocodone containing products?

**Answer:**

The cited reference reports “The change in scheduling for hydrocodone combination products has resulted in more restrictive prescribing regulations. Refills are no longer allowed. Prescriptions that were filled before October 6, 2014, may be allowed to be refilled until April 7, 2015.” Further “prescriptions for hydrocodone combination products must be written; these products cannot be prescribed over the phone or by fax.” In addition “Many states have additional laws that limit the quantity of a schedule II drugs that can be prescribed on a single prescription, and some states do not allow physician assistants, nurse practitioners or optometrists to prescribe schedule II controlled substances. (The Medical Letter, October 13, 2014, 56(1453): 102)

**Tuesday, October 21, 2014****Question:**

There are currently three SGLT2 (sodium-glucose co-transporter 2) inhibitors approved by the FDA for oral treatment of type 2 diabetes. What are they and what are the reported adverse effects of these drugs?

**Answer:**

The currently approved SGLT2 inhibitors are: Canagliflozin (Invokana), Dapagliflozin (Farxiga) and Empagliflozin (Jardiance). According to the cited reference, these drugs have "been associated with genitourinary symptoms and genital mycotic infections". These drugs also have a "modest diuretic effect and that could lead to dehydration, hypovolemia and hypotension, particularly in elderly associated with renal dysfunction or who are taking a diuretic." (The Medical Letter October 13, 2014, 56(1453):99-100)

**Monday, October 20, 2014**

**Question:**

There are currently three SGLT2 (sodium-glucose co-transporter 2) inhibitors approved by the FDA for oral treatment of type 2 diabetes. What are they and what are the reported adverse effects of these drugs?

**Answer:**

There are currently three SGLT2 (sodium-glucose co-transporter 2) inhibitors approved by the FDA for oral treatment of type 2 diabetes. What are they and what are the reported adverse effects of these drugs?

**Friday, October 17, 2014**

**Question:**

What are the most common emergency department presenting complaints in patients who abuse ketamine?

**Answer:**

One study of 20 patients reported “the majority of ketamine abusers visit the ED with complaints of anxiety, chest pain, palpitations, confusion and memory loss. Observed physical symptoms are hypertension, tachycardia, nystagmus, hallucinations and slurred speech”. (Weiner AL et al. Ketamine abusers presenting to the emergency department: a case series. 2000J Emerg Med; 18: 447–51 as cited in Niesters M et al. Ketamine for chronic pain: risks and benefits. 2013 Brit J Clin Pharmacology 77(2): 357-367)

**Thursday, October 16, 2014**

**Question:**

A wide variety of drugs have been reported to cause immune cytopenias including heparin, penicillin and its derivatives, abciximab, quinidine, and quinine. What is the typical clinical presentation for quinine induced thrombocytopenia? What are the characteristics of the antibodies responsible for quinine induced thrombocytopenia?

**Answer:**

The authors of the cited reference state, “The antibodies responsible for quinine-induced thrombocytopenia (QITP) are immunoglobulins that usually recognize the VWF or the fibrinogen receptors glycoprotein (GP) Ib/IX or GPIIb/IIIa. Quinine-dependent antibodies are notable by the fact that they have no significant affinity for the platelet antigen unless the drug is present at therapeutic concentrations. Typically, patients with QITP present with severe thrombocytopenia (platelet count  $< 10 \times 10^9/L$ ) of abrupt onset after a variable period of taking quinine; they often have petechiae and mucosal bleeding. After cessation of the offending drug, the platelet counts usually increase to above baseline levels generally after a week but occasionally may require longer recovery periods.” (Perdomo J et al. Quinine-induced thrombocytopenia: drug-dependent GPIb/IX antibodies inhibit megakaryocyte and proplatelet production in vitro. 2011 Blood 117(22):5975-5986)

**Wednesday, October 15, 2014**

**Question:**

What is the association between the development of atrial fibrillation and the administration of bisphosphonates?

**Answer:**

A recently published meta-analysis concluded “Evidence from randomized controlled trials and observational studies suggests a significantly increased risk of atrial fibrillation requiring hospitalization, but no increase in risk of stroke or cardiovascular mortality, with the use of bisphosphonate”. (Sharma A et al. Risk of serious atrial fibrillation and stroke with use of bisphosphonates: Evidence from a meta-analysis. 2013 Chest 144(4): 1311-1322)

**Tuesday, October 14, 2014**

**Question:**

What is the pathophysiology of prolonged skin exposure to chloroform (trichloromethane) and/or related hydrocarbons?

**Answer:**

The cited reference notes that “prolonged dermal exposure” to chloroform “can cause a defatting dermatitis as epidermal lipids are destroyed”. (Greene SC and White NR. Images in Emergency Medicine. 2014 Ann Emerg Med 64(3) pages 231 and 247)

**Monday, October 13, 2014**

**Question:**

What are the factors associated with an increased risk for the development of agranulocytosis in patients taking the antipsychotic drug clozapine?

**Answer:**

The cited reference notes “Increasing age and female gender are both independently associated with an increased risk of agranulocytosis with clozapine”. The authors further emphasize that “It has been suggested that older patients are 10–16 times more likely to develop agranulocytosis with clozapine than their younger counterparts and that they are more likely to die when agranulocytosis occurs”. (Bishara D and Taylor D. Adverse effects of clozapine in older patients: Epidemiology, prevention and management. 2014 Drugs Aging 31:11-20)

**Friday, October 10, 2014**

**Question:**

The illicit use of ketamine has been reported to cause a certain genitourinary problem characterized by severe dysuria, frequency, urgency and gross hematuria. What is this problem and what is the purported cause?

**Answer:**

This is the so-called ketamine associated ulcerative cystitis. Studies have shown that high concentrations of ketamine and metabolites norketamine and hydroxynorketamine concentrate in the urine following ketamine use. It has been posited that these chemicals may, in some cases, induce bladder irritation as well as some cases of bladder ulceration. (Shahani R et al. Ketamine associated ulcerative cystitis: A new clinical entity. 2007 Urology 69(5): 810-812)

**Thursday, October 9, 2014**

**Question:**

What are the commonly use synonyms for the chemical tetrachloroethylene?

**Answer:**

Other names for tetrachloroethylene include perchloroethylene, PCE, perc, tetrachloroethene, perclene, and perchlor. (<http://www.atsdr.cdc.gov/PHS/PHS.asp?id=263&tid=48>; accessed July, 2014)

**Wednesday, October 8, 2014**

**Question:**

What is the relationship between the use of bisphosphonates (e.g. alendronate, ibandronate, risedronate) and the development of esophageal cancer?

**Answer:**

The cited reference indicates "Some reports have suggested an association between the use of bisphosphonates and esophageal cancer, but the data have been conflicting. The FDA has not concluded that these agents increase the risk of esophageal cancer, but has recommended that they not be used in patients with Barrett's esophagus." (The Medical Letter, September 29, 2014, 56(1452): 91-96)

**Tuesday, October 7, 2014**

**Question:**

What is the phenomenon known as the "K-hole" and what drug is commonly associated with the so-called K-hole?

**Answer:**

The cited reference notes: "At low doses ketamine induces distortion of time and space, hallucinations and mild dissociative effects. However, at large doses (i.e. over 150 mg) ketamine induces more severe dissociation commonly referred to as a "K hole", wherein the user experiences intense detachment to the point that their perceptions appear located deep within their consciousness, thus causing reality to appear far off in the distance." (Muetzelfeldt L., et al. Journey through the K-hole: Phenomenological aspects of ketamine use. 2008 Drug and Alcohol Dependence. 95:219-229)

**Monday, October 6, 2014**

**Question:**

What is the phenomenon, usually applied to medication efficacy, when "negative effects on treatment efficacy and tolerability are induced or driven by psychological factors"?

**Answer:**

The above-described phenomenon is the so-called "nocebo effect". (Bingel U. Avoiding nocebo effects to optimize treatment outcome. 2014 JAMA 312(7):693-694)

**Friday, October 3, 2014**

**Question:**

What is the difference between pyrethrins and pyrethroids?

**Answer:**

Pyrethrins are naturally occurring compounds with insecticidal properties that are found in pyrethrum extract from certain chrysanthemum flowers. The pyrethrins are often used in household insecticides and products to control insects on pets or livestock. Pyrethroids are manufactured chemicals that are very similar in structure to the pyrethrins, but are often more toxic to insects as well as to mammals, and last longer in the environment than the pyrethrins. More than 1,000 synthetic pyrethroids have been developed, but less than a dozen of them are currently used in the United States. Permethrin is the most frequently used pyrethroid in the United States. (<http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=153>; accessed September, 2014)

**Thursday, October 2, 2014**

**Question:**

Common adverse effects of isoniazid involve the liver. While a mild elevation of transaminase enzymes occurs in roughly 15-20% of patients receiving this drug what proportion of treated patients go on to develop clinical hepatitis and what percentage may be expected to develop fatal hepatitis?

**Answer:**

Clinical hepatitis may develop in up to 2.0 % of patients and fatal hepatitis may develop in up to 0.001% of patients. (Science M et al. Isoniazid toxicity in a 5-year old boy. 2013 CMAJ 185(10): 894-896)

**Wednesday, October 1, 2014**

**Question:**

What are the common symptoms associated with exposure of human skin to jellyfish tentacles ([sea nettle (*Chrysaora quinquecirrha*), Portuguese man-of-war — (*Physalia* spp.), hydroid (*Lytocarpus philippinus* sp.), and mauve stinger (*Cyanea capillata*])) and what is the most effective post-exposure treatment?

**Answer:**

According to the cited reference, "Symptoms of humans exposed to jellyfish tentacles are pain, localized areas of swelling, redness and bleeding." These authors go on to state "Some of the chemicals traditionally used to treat jellyfish stings in humans include dilute acetic acid (vinegar), sodium bicarbonate (baking soda), ammonia, papain or bromelain (meat tenderizer), ethanol and salt water." In the cited study, the authors report "that many of the chemicals traditionally used to treat jellyfish stings stimulated nematocyst discharge and did not relieve the pain." They found that "lidocaine, in addition to acting as an anesthetic on skin in contact with jellyfish tentacles, inhibited nematocyst discharge possibly by blocking sodium and/or calcium channels of the nematocytes." (Birsá LM et al. Evaluation of the effects of various chemicals on discharge of and pain caused by jellyfish nematocysts. 2010 Comparative Biochemistry and Physiology, Part C 151:426-430)

**Tuesday, September 30, 2014**

**Question:**

What is guthion?

**Answer:**

Guthion, also called azinphos-methyl, is an organophosphorous pesticide that was used on many crops, especially apples, pears, cherries, peaches, almonds, and cotton. Many of its former uses have been cancelled by the EPA, and its few remaining uses are currently in the process of being phased out. Guthion is a synthetic substance, it does not occur naturally. Pure guthion is a colorless to white odorless crystalline solid that melts at about 72-74°C (162-165°F). Technical-grade guthion is a cream to yellow-brown granular solid. Guthion is poorly soluble in water. (<http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=207>; accessed August, 2014)

**Monday, September 29, 2014****Question:**

The risk for congenital anomalies in pregnant females taking lithium is generally considered to be high. Which congenital cardiac anomaly has been reported to be associated with a 400-fold increased risk in pregnancies where the mother took lithium for a substantial portion of their pregnancy?

**Answer:**

A 400-fold increased risk for Ebstein's anomaly has been reported when lithium was taken during pregnancy. (Nora JJ, et al. Lithium, Ebsteins anomaly, and other congenital heart defects. 1974 Lancet, 304: 594-95 as cited in McKnight R et al. Lithium toxicity profile: a systematic review and meta-analysis. 2012 Lancet, 379:721-728)

**Friday, September 26, 2014****Question:**

A variety of non-instrumentation, so-called field sobriety tests, are used by law enforcement across the USA and around the world. What is the reliability of these tests in discerning ethanol intoxication (e.g. "hand pat" test, "finger-to-finger" test, "finger-to-nose" test)?

**Answer:**

The cited reference notes: "All of the sobriety tests have been the subject of remarkably few published, peer-reviewed studies, and most show weak correlations with BACs below .15%." (Rubenzer S. Judging intoxication. 2011 Behav Sci Law 29:116-137)

**Thursday, September 25, 2014****Question:**

Millipedes are arthropods that do not bite or sting. How do millipedes produce the exposure effects of pain, burning and skin discoloration?

**Answer:**

The cited reference explains that these animals "produce an irritating defensive substance that is secreted through pores located on the lateral aspect of each [body] segment." The author further notes "The exact components of the secretion depend on the species of millipede but include phenols, benzoquinones, hydrogen cyanide, aldehydes, terpenoids, and nitroethylbenzenes." (Hendrickson RG. Millipede exposure. 2005 Clin Tox 43(3):211-212)

**Wednesday, September 24, 2014****Question:**

The intermediate syndrome is a delayed-onset of muscular weakness and paralysis following an episode of acute cholinesterase inhibitor poisoning. How long after exposure does the so-called "intermediate syndrome" develop?

**Answer:**

The intermediate syndrome most commonly develops 24-96 hours after resolution of the acute cholinergic toxidrome. (<http://www.atsdr.cdc.gov/csem/csem.asp?csem=11&po=28>; accessed September, 2014)

**Tuesday, September 23, 2014****Question:**

What was the toxicant involved in the so-called Massengil tragedy?

**Answer:**

The Massengil tragedy occurred in 1937 when more than 100 deaths were documented related to the use of sulphanilamide elixir suspended in diethylene glycol. "Massengil" refers to the Massengil Company of Bristol, Tennessee. This incident hastened the enactment of the 1938 Federal Food Drug and Cosmetic Act, the statute that remains the basis for FDA regulation of these products. (Alfred S et al. Delayed neurologic sequelae resulting from epidemic diethylene glycol poisoning. 2005 Clin Tox 43(3):155-159)

**Monday, September 22, 2014****Question:**

What are the common facial features in infants with fetal hydanotin syndrome (FHS)?

**Answer:**

The facial features commonly seen in infants with FHS include a flat nasal bridge, bilateral downward slanting eyes, wide-spaced eyes that may demonstrate strabismus and ptosis. A poorly developed philtrum as well as cleft lip and/or palate may also be present. (<http://www.rarediseases.org/rare-disease-information/rare-diseases/byID/948/viewFullReport>; accessed September 2014)

**Friday, September 19, 2014**

**Question:**

What is the association between long-term exposure to arsenic in drinking water and the development of QTc interval prolongation?

**Answer:**

The cited systematic review notes “in the Normative Aging Study, an interquartile range increase in toenail arsenic, a biomarker of long-term exposure to arsenic, was associated with a 3.8 millisecond increase in QT interval (95 % CI: 0.82–6.8) and a 2.5 millisecond increase in QTc (heart rate-corrected QT) interval (95 % CI: 0.11–4.9).” (Mumford JL et al. Chronic arsenic exposure and cardiac repolarization abnormalities with QT interval prolongation in a population-based study. 2007 Environ Health Perspect. 115(5): 690–694, as cited in Moon et al. Arsenic exposure and cardiovascular disease: An updated systematic review 2012 Curr Atheroscler Rep 14: 542-555)

**Thursday, September 18, 2014**

**Question:**

Phenol (carbolic acid C6H6O) is used as a disinfectant, an industrial feedstock chemical for a variety of synthetic reactions and as an ingredient in a variety of medicinal products including Anbesol, Campho-phenique and Chloroseptic. It is also used as an injectable in sympathetic nerve blocks and in so-called chemical peels. What are the potential toxicities associated with phenol exposure?

**Answer:**

The cited reference notes “Phenol causes severe irritation and corrosion on skin contact [or contact with] other tissues. It is a caustic and causes injury by coagulative necrosis. Systemic absorption has been documented to produce cyanosis, shock, weakness, cardiac arrhythmia, collapse and convulsion, liver and kidney failure, coma, and death.” These authors further note, “Phenol has excellent dermal penetration and topical exposure has resulted in severe burns as well as severe systemic toxicity.” (Philip AT and Marraffa JM. Death following injection sclerotherapy due to phenol toxicity. 2012 J Forensic Sci 57(5):1372-1375)

**Wednesday, September 17, 2014**

**Question:**

In 2004, formaldehyde was classified by IARC as a “human carcinogen”. What was the basis for this classification and what form of cancer did IARC promulgate as being caused by certain formaldehyde exposures?

**Answer:**

According to the cited reference, “The literature was reviewed by IARC in 2004 and formaldehyde was classified as a Human Carcinogen, based on an increase in nasopharyngeal cancer (NPC) in the National Cancer Institute (NCI) cohort of >25,000 formaldehyde workers in 10 plants.” In 2012, IARC reiterated its position that formaldehyde causes nasopharyngeal cancer. Nonetheless a number of large cohort studies have not shown clear causation for NPC associated with formaldehyde exposures and the notion that formaldehyde causes NPC remains controversial. (Swenberg JA et al. Formaldehyde carcinogenicity research: 30 years and counting for mode of action, epidemiology and cancer risk assessment. 2013 Toxicologic Path 41(2): 181-189)

**Tuesday, September 16, 2014**

**Question:**

What is aegeline and what clinical problems has it been implicated as causing?

**Answer:**

According to the cited resource, “aegeline is a new ingredient being added to dietary supplements; it can also appear on a product label as N-[2-hydroxy-2(4-methoxyphenyl)ethyl]-3-phenyl-2-propenamide. Aegeline is a compound extracted from Aegle marmelos (bael), a plant that has a long history of use in Ayurvedic medicine. Although some evidence from animal studies suggests that aegeline might lower blood sugar, this potential effect has never been studied in humans. This compound has been used as an ingredient in weight-loss aid products too, but again there is no evidence that it is effective for weight loss in humans.”

The cited resource further notes that “FDA recently issued an information update stating that FDA along with the Centers for Disease Control and Prevention are investigating more than 50 cases of liver damage. FDA also issued a warning letter to a company marketing a dietary supplement that contains aegeline, because it is not currently recognized as a legitimate ingredient for dietary supplements.”

(<http://hprc-online.org/dietary-supplements/opss/operation-supplement-safety-OPSS/opss-frequently-asked-questions-faqs-1/what-is-aegeline-and-why-is-it-a-problem/>; accessed September, 2014)

**Monday, September 15, 2014**

**Question:**

What is ANSI? What does ANSI do?

**Answer:**

“ANSI” is the American National Standards Institute. This organization, founded in 1918, oversees the creation, promulgation and use of thousands of norms and guidelines that directly impact businesses in nearly every sector: from acoustical devices to construction equipment, from dairy and livestock production to energy distribution, and many more. ANSI is also actively engaged in accrediting programs that assess conformance to standards – including globally-recognized cross-sector programs such as the ISO 9000 (quality) and ISO 14000 (environmental) management systems. ([ansi.org/about\\_ansi/overview/overview.aspx?menuid=1](http://ansi.org/about_ansi/overview/overview.aspx?menuid=1); accessed September, 2014)

**Friday, September 12, 2014**

**Question:**

What is the Household Products Database?

**Answer:**

The Household Products Database is sponsored by the National Library of Medicine and is based on the Consumer Product Information Database. This database links over 14,000 consumer brands to health effects from Material Safety Data Sheets (MSDS) provided by manufacturers and allows scientists and consumers to research products based on chemical ingredients. The database is designed to help answer the following typical questions:

- What are the chemical ingredients and their percentage in specific brands?
- Which products contain specific chemical ingredients?
- Who manufactures a specific brand? How do I contact this manufacturer?
- What are the acute and chronic effects of chemical ingredients in a specific brand?
- What other information is available about chemicals in the toxicology-related databases of the National Library of Medicine? (<http://hpd.nlm.nih.gov/about.htm>; accessed September, 2014)

**Thursday, September 11, 2014**

**Question:**

Alzheimer's dementia is predicted to affect more than 150 million individuals worldwide by the year 2050. Benzodiazepines have been investigated as having a possible causative role in the development of this devastating disease. What is the association between the development of Alzheimer's dementia and the taking of benzodiazepine drugs?

**Answer:**

A recently completed case-control study of 1796 individuals diagnosed with Alzheimer's disease matched with 7184 controls has been published. The investigators have reported as follows. "Benzodiazepine ever use was associated with an increased risk of Alzheimer's disease (adjusted odds ratio 1.51, 95% confidence interval 1.36 to 1.69; further adjustment on anxiety, depression, and insomnia did not markedly alter this result: 1.43, 1.28 to 1.60). No association was found for a cumulative dose <91 prescribed daily doses. The strength of association increased with exposure density (1.32 (1.01 to 1.74) for 91-180 prescribed daily doses and 1.84 (1.62 to 2.08) for >180 prescribed daily doses) and with the drug half life (1.43 (1.27 to 1.61) for short acting drugs and 1.70 (1.46 to 1.98) for long acting ones)." (Billiot de Gage, S. et al. Benzodiazepine use and risk of Alzheimer's disease: case-control study. BMJ 2014;349: g5205)

**Wednesday, September 10, 2014**

**Question:**

What is the therapeutic rationale for the use of hyperbaric oxygen (HBO) in the treatment of individuals with severe exposure to hydrogen sulfide?

**Answer:**

The cited reference reports "The theory behind HBO use rests on competitively inhibiting the sulfide-cytochrome-aa3 interaction. Oxygen competes with hydrogen sulfide for binding sites on cytochrome-aa3. HBO therapy saturates tissues with oxygen and favors the cytochrome-aa3-oxygen interaction over the cytochrome-aa3-sulfide interaction." (Gerasimon G et al. Acute hydrogen sulfide poisoning in a dairy farmer. 2007 Clin Tox 45(4): 420-423)

**Tuesday, September 9, 2014**

**Question:**

Tramadol, an opioid agonist may be used to treat moderate to moderately severe pain. This drug also inhibits the reuptake of norepinephrine and serotonin. What are the adverse effects associated with the use of this drug that may result in patients discontinuing its use?

**Answer:**

The cited reference notes "a substantial minority of patients discontinued [tramadol] because of adverse effects that included nausea, vomiting, constipation, dizziness and somnolence. Seizures have occurred with tramadol and physical dependence has been reported." (The Medical Letter September 1, 2014, 56(1450):83)

**Monday, September 8, 2014**

**Question:**

Ondansetron is a commonly used antiemetic agent that acts by antagonizing serotonin at 5-hydroxytryptamine-3 receptors. The FDA has warned that ondansetron may induce fatal arrhythmias. What is the risk for arrhythmia induction following a single oral ondansetron dose?

**Answer:**

A recently published postmarketing analysis and systematic review reported "no reports describing an arrhythmia associated with single oral ondansetron dose administration." However, given the fact that this drug is frequently administered intravenously the authors of the cited study remind readers that high dose ondansetron given intravenously may prolong the QT interval and should be cautiously administered in patients with a significant medical history or who are also using any medication capable of causing QT prolongation.(Freedman SB et al. Ondansetron and the risk of cardiac arrhythmias: A systematic review and postmarketing analysis. 2014 Ann Emerg Med 64(1):19-25)

**Friday, September 5, 2014**

**Question:**

What is the so-called "gateway hypothesis" with regard to illicit drug use?

**Answer:**

The cited reference notes "The gateway hypothesis was developed by Denise Kandel, who observed that young people become involved in drugs in stages and sequences." Dr. Kandel observed that in the United States and other Western societies, "a well-defined developmental sequence of drug use occurs that starts with a legal drug and proceeds to illegal drugs." Thus, it has been noted that "the use of tobacco or alcohol precedes the use of marijuana, which in turn precedes the use of cocaine and other illicit drugs." (Kandel DB. Stages in adolescent involvement in drug use. Science 1975;190: 912-914 as quoted in Kandel ER and Kandel DB. A molecular basis for nicotine as a gateway drug. 2014 NEJM 371:932-943)

**Thursday, September 4, 2014**

**Question:**

Ingestion of amatoxin-containing mushrooms accounts for the vast majority of deaths attributable to mushroom ingestion on a worldwide basis. What are the major amatoxins, what is their most likely mechanism of action and which amatoxin is thought to be primarily responsible for human disease due to the ingestion of amatoxin containing mushrooms?

**Answer:**

The authors of the cited reference note that "There are currently 10 known amatoxins with molecular weights of approximately 900 Daltons." They go on to state "The major amatoxins, the alpha-, beta-, and gamma-amanitins, damage the liver and kidney via irreversible binding to RNA polymerase II. Of these, alpha-amanitin is thought to be primarily responsible for human disease." (Trabulus S and Altiparmak MR. Clincila features and outcome of patients with amatoxin-containing mushroom poisoning. 2011 Clin Tox 49(4): 303-310)

**Wednesday, September 3, 2014**

**Question:**

Dieffenbachia, also known as "dumbcane", "dumb plant" and "mother-in-law's tongue" is a common houseplant that may cause significant mucosal tissue injury when oral contact occurs with stems or leaves or when ocular or dermal contact occurs. What is the mechanism of toxicity involved in the injuries resulting from oral exposure to this plant?



**Answer:**

A specific mechanism of toxicity has yet to be elucidated. The authors of the cited reference state “The mechanism of toxicity seems to be multifaceted. Raphides, idioblasts, and another unidentified proteinaceous or non-proteinaceous substance all contribute in some degree to Dieffenbachia toxicity.” (Cumpston KL et al. Acute airway compromise after brief exposure to a dieffenbachia plant. 2003 J Emerg Med 25(4): 391-397)

**Tuesday, September 2, 2014****Question:**

What is blarina toxin?

**Answer:**

The authors of the cited study state “Blarina toxin is a potent mammalian venom with a tissue kallikrein-like activity from the submaxillary and sublingual glands of the shorttailed shrew Blarina brevicauda.” These authors go on to state that “Among mammals, the short-tailed shrew B. brevicauda is well known to produce this venom in its saliva, which is toxic to mammals, such as mice, voles, rabbits, and cats. Human accounts of bites from Blarina describe a local burning sensation around the tooth puncture marks and subsequent swelling.” (Kita M et al. Blarina toxin, a mammalian lethal venom from the short-tailed shrew Blarina brevicauda: Isolation and characterization. 2004 PNAS 101(20): 7542–7547)

**Monday, September 1, 2014****Question:**

How is the product known as “Crofab” (Crotalidae Polyvalent Immune Fab (Ovine)) produced? Which crotalid, found on the West Coast of the United States, is not included in the manufacturing process for Crofab?

**Answer:**

The cited reference reports “CroFab is a purified Fab (monovalent) immunoglobulin obtained from the blood of healthy sheep immunized with 1 of 4 North American pit vipers. These include the Western diamondback rattlesnake (Crotalus atrox), Eastern diamondback rattlesnake (Crotalus adamanteus), Mojave rattlesnake (Crotalus scutulatus), and cottonmouth water moccasin (Agkistrodon piscivorus).” The authors go on to report that “Each immunoglobulin is fractionated from the sheep serum and digested with papain, and the venom-specific Fab fragments are separated with affinity chromatography and ion exchange. These 4 monospecific antivenoms are then mixed to produce the final compound.” Ovine-derived antivenom is not made from the venom of the Southern Pacific Coast rattlesnake (C. Helleri) (Walker JP and Morrison RL. Current management of copperhead snakebite. 2011 J Am Coll Surg 212:470–475)

**Friday, August 29, 2014****Question:**

Aristolochic acid containing herbals have been implicated in the development of what chronic medical problem?

**Answer:**

Aristolochic acid containing herbals have been implicated in the development of renal interstitial fibrosis with renal failure. Some reports also implicate this substance in the development of urothelial carcinoma. (Ko R. Safety of ethnic and imported herbal and dietary supplements. 2006 Clin Tox 44:611-616)

**Thursday, August 28, 2014****Question:**

Selegiline is a selective MAO-B inhibitor that blocks the breakdown of dopamine in the brain. This drug was the first MAO-B inhibitor used in the treatment of Parkinson disease and has recently been reconsidered as a primary treatment for Parkinson Disease. What issue may arise when individuals taking this drug undergo urine drug testing?

**Answer:**

The cited reference points out that selegiline is metabolized into the active metabolites desmethyl-selegiline, L-methamphetamine, and L-amphetamine and thus may confound routine immunoassay drug screens for amphetamine and/or methamphetamine. (Fabbrini G et al. Selegiline: A reappraisal of its role in Parkinson Disease. 2012 Clin Neuropharm 35:134-140)

**Wednesday, August 27, 2014****Question:**

What are the cancer risks related to occupational exposure to Portland cement?

**Answer:**

A recently published meta-analysis analyzed 26 studies (14 occupaoptinal cohort studies and 12 case-control studies). According to the authors of the cited study, “Overall, the meta-relative risks calculated across 26 published studies do not provide evidence of increased risks for cancer in relation to cement exposure.” (Cohen SS et al. A review and meta-analysis of cancer risks in relation to Portland cement exposure. 2014 Occup Environ Med Aug 20. pii: oemed-2014-102193. doi: 10.1136/oemed-2014-102193. [Epub ahead of print])

**Tuesday, August 26, 2014****Question:**

What is phototoxic dermatitis?

**Answer:**

According to the cited reference, phototoxic dermatitis is “an inflammatory, photochemically evoked skin reaction caused by concomitant exposure to sun and photosensitizing substances (furocoumarins are one such group) which increase the reactivity of skin to ultraviolet radiation.” (Zink A and Ring J. Phototoxic dermatitis. 2014 NEJM 371:6)

**Monday, August 25, 2014****Question:**

What is the World Anti-Doping Code?

**Answer:**

According to the U.S. Anti-Doping Agency, “The Code is a core document that provides the framework for anti-doping policies, rules, and regulations within sport organizations and among public authorities. It is designed to harmonize anti-doping policies and ensure the standards are the same for all athletes. The Code works in conjunction with five international standards that further provide guidelines for anti-doping efforts.” (<http://www.usada.org/about/world-anti-doping-code/>; accessed August, 2014)

**Friday, August 22, 2014****Question:**

What is the pathophysiology of acute renal failure in ethylene glycol poisoning?

**Answer:**

The cited reference notes “Although the “aldehyde” metabolites of ethylene glycol, glycolaldehyde and glyoxalate, have been suggested as the metabolites responsible, recent studies have shown definitively that the accumulation of calcium oxalate monohydrate (COM) crystals in the kidney tissue produces renal tubular necrosis that leads to kidney failure.” (McMartin K. Are calcium oxalate crystals involved in the mechanism of acute renal failure in ethylene glycol poisoning? 2009 Clin Tox 47(9):859-869)

**Thursday, August 21, 2014****Question:**

Bedaquiline has recently been approved to treat adults with multidrug resistant pulmonary tuberculosis. What is the mechanism of action for this drug?

**Answer:**

According to the cited reference, “Bedaquiline is an antimycobacterial drug that operates by a new mechanism of action: it inhibits mycobacterial ATP synthetase and depletes cellular energy stores. Since its mechanism differs from those of other available antimycobacterial drugs, it has the capacity to retain activity against some M. tuberculosis isolates that are resistant to other drugs and hence may provide an important treatment option for patients with multidrug-resistant pulmonary tuberculosis when an effective multidrug treatment regimen cannot otherwise be constructed.” (Cox E and Laessig K. FDA approval of bedaquiline- The benefit-risk balance for drug resistant tuberculosis. 2014 NEJM 371(8):689-691)

**Wednesday, August 20, 2014****Question:**

What are the generally accepted characteristics of a “cancer cluster”?

**Answer:**

According to the CDC in order to be a cancer cluster, a group of cancer cases must meet the following criteria:

A greater than expected number: A greater than expected number is when the observed number of cases is higher than one would typically observe in a similar setting (in a group with similar population, age, race, or gender). This may involve comparison with rates for comparable groups of people over a much larger geographic area – e.g., an entire state.

Of cancer cases: All of the cases must involve the same type of cancer, or types of cancer scientifically proven to have the same cause.

That occurs within a group of people: The population in which the cancers are occurring is carefully defined by factors such as race/ethnicity, age, and gender, for purposes of calculating cancer rates.

In a geographic area: Both the number of cancer cases included in the cluster and calculation of the expected number of cases can depend on how we define the geographic area where the cluster occurred. The boundaries must be defined carefully. It is possible to “create” or “obscure” a cluster by selection of a specific area.

Over a period of time: The number of cases included in the cluster – and calculation of the expected number of cases – will depend on how we define the time period over which the cases occurred. (<http://www.cdc.gov/nceh/clusters/default.htm>; accessed June, 2014)

**Tuesday, August 19, 2014****Question:**

What is ethion?

**Answer:**

Ethion (C9H22O4P2S4) is an organophosphate pesticide. Pure ethion is a clear to yellowish liquid with an unpleasant sulfur-like smell. It does not occur naturally in the environment. Ethion is used in agriculture, mainly to control insects on citrus trees, but also on cotton, fruit and nut trees, and some vegetables. It may also be used on lawns and turf grasses, but it is not used in the home for pest control. (<http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=206>, accessed July 2014)

**Monday, August 18, 2014****Question:**

The cited reference notes that “Immune reaction in drug mediated thrombotic microangiopathy was first recognized in 1980 in a patient who had repeated episodes of acute kidney injury, hemolysis and thrombocytopenia after documented exposures” to what drug?

**Answer:**

“Immune reaction in drug mediated thrombotic microangiopathy was first recognized in 1980 in a patient who had repeated episodes of acute kidney injury, hemolysis and thrombocytopenia after documented exposures” to quinine. (George JN and Nester CM. Syndromes of thrombotic microangiopathy. 2014 NEJM 371(7): 654-666)

**Thursday, August 14, 2014****Question:**

Acrolein is a highly reactive aldehyde contained in cigarette smoke, cotton smoke, wood smoke and coal smoke as well as gasoline and diesel exhaust. Which biomarker has been used to assess exposure to acrolein?

**Answer:**

The measurement of urinary levels of the major acrolein metabolite, 3-hydroxypropylmercapturic acid (3-HPMA) is the most commonly used biomarker for exposure to acrolein. (Dejarnett N et al. Acrolein exposure is associated with increased cardiovascular disease risk. J Am Heart Assoc. 2014 Aug 6;3(4). pii: e000934. doi: 10.1161/JAHA.114.000934)

**Wednesday, August 13, 2014**

**Question:**

There are currently three TNF (tumor necrosis factor) inhibitors used to treat moderate to severe Crohn's disease. What are these drugs and what are the adverse effects associated with their use?

**Answer:**

The TNF (tumor necrosis factor) inhibitors used to treat severe Crohn's disease are infliximab (Remicade), adalimumab (Humira) and certolizumab pegol (Cimzia). According to the cited reference, these agents have been "associated with injection and infusion reactions and new onset psoriasis, hematologic cytopenias, non-ischemic congestive heart failure, demyelinating disorders, and induction of a lupus-like syndrome." In addition, an increased risk of a variety of cancers has been reported with the use of TNF inhibitors but causation has yet to be proven in this regard. (The Medical Letter, 56(1448): 59-66)

**Tuesday, August 12, 2014**

**Question:**

What are the effects of long-term marijuana smoking on the risk for developing lung cancer?

**Answer:**

According to a recent review "The effects of long-term marijuana smoking on the risk of lung cancer are unclear. For example, the use of marijuana for the equivalent of 30 or more joint-years (with 1 joint-year of marijuana use equal to 1 cigarette [joint] of marijuana smoked per day for 1 year) was associated with an increased incidence of lung cancer and several cancers of the upper aerodigestive tract; however, the association disappeared after adjustment for potential confounders such as cigarette smoking. Although the possibility of a positive association between marijuana smoking and cancer cannot be ruled out, the evidence suggests that the risk is lower with marijuana than with tobacco." (Volkow ND et al. Adverse health effects of marijuana use. 2014 NEJM 370(23):2219-2227)

**Monday, August 11, 2014**

**Question:**

What is the Beryllium Biobank (BBB)?

**Answer:**

According to the cited reference, the BBB is "a repository of clinical data and biologic specimens collected from the US Department of Energy (DOE) workers and contractors with possible beryllium exposure. The BBB data include extensive radiographic, immunologic, physiologic, symptom, examination, and other test information, in addition to LPT results. The data were collected in a highly systematic fashion from people with diverse potential exposures to facilitate research about beryllium-related health matters." (Harber P. et al. Exposure factors associated with chronic beryllium disease development in beryllium biobank participants. 2014 J Occ Env Med 56(8):852-856)

**Friday, August 8, 2014**

**Question:**

What is alachlor? What is butachlor?

**Answer:**

Alachlor (trade name "Lasso") is an aniline herbicide widely used in the USA, South America and Asia to control grasses and broad-leaf weeds. Butachlor is an analog of alachlor. Both are mucous membrane irritants that may, in some cases, cause severe neurological and cardiovascular effects if ingested in large quantities. (Lo Y, et al. Acute alachlor and butachlor herbicide poisoning. 2008 Clin Tox 46(8): 716-721)

**Thursday, August 7, 2014**

**Question:**

What was the original rationale for the development of the drug carisoprodol?

**Answer:**

The cited reference notes that carisoprodol was introduced in the late 1950's "as an alternative to meprobamate, hoping that it would have less sedative and better muscle relaxing properties. However the drugs turned out to have many clinical similarities, possibly explained by the fact that carisoprodol is almost completely metabolized to meprobamate by dealkylation. (Brames JG and Morland J. Carisoprodol intoxications and serotonergic features. 2005 Clin Tox 43(1): 39-45)

**Wednesday, August 6, 2014**

**Question:**

What is the effect of the administration of hydroxocobalamin (B12a) on carboxyhemoglobin?

**Answer:**

The authors of the cited reference studied this question in vitro and concluded: "The magnitude of B12a interference on measured COHb is dependent upon the specific co-oximeter used, the actual COHb level and the serum B12a concentration. These errors may potentially influence clinical decision making and thus affect patient outcomes." As a result, these authors recommend "measuring COHb levels on blood samples collected prior to B12a administration". (Pace R et al. Effects of hydroxocobalamin on carboxyhemoglobin measured under physiologic and pathologic conditions. 2014 Clin Tox 52(7): 647-650)

**Tuesday, August 5, 2014**

**Question:**

What is the ATSDRs Rapid Response Registry (RRR)?

**Answer:**

The ATSDRs RRR helps local and state public health and disaster response agencies rapidly establish registries of persons who are exposed or potentially exposed to chemicals or other harmful agents during catastrophic events. ATSDR's RRR survey instrument gives local and state entities a tool to register responders and other persons exposed to chemical, biological, or nuclear agents from a disaster. The survey instrument is a two-page form that can be distributed on paper or electronically. It can be implemented quickly to collect information rapidly to identify and locate victims and people displaced or affected by a disaster. For mass casualty events, ATSDR identified four critical fields that would be sufficient to establish an official registry record and require only about 90 seconds to complete for each registrant. These are the registrant's name, gender, home address, and telephone numbers.(<http://www.atsdr.cdc.gov/rapidresponse/>; accessed June, 2014)

**Monday, August 4, 2014****Question:**

There is a current water emergency in the Toledo, Ohio area involving algal bloom related toxins in the drinking water supply. What is the nature of these toxins?

**Answer:**

The relevant toxins are so-called cyanotoxins. The cited reference notes these are "ubiquitous microorganisms considered as important contributors to the formation of Earth's atmosphere and nitrogen fixation. However, they are also frequently associated with toxic blooms. Indeed, the wide range of hepatotoxins, neurotoxins and dermatotoxins synthesized by these bacteria is a growing environmental and public health concern." Specifically, the Toledo events concern microcystins. The authors of the cited reference go on to describe that "Microcystins (MCs) form the main family of cyanotoxins since they are the most frequently studied and the most widespread." Microcystins inhibit the enzyme protein phosphatase and have been associated with liver failure and hepatic hemorrhage (primarily in experimental animals). One infamous event involving these toxins took place in Brazil in 1996 when water containing this toxin was used for hemodialysis and resulted in the death of 60 patients at one dialysis center. (Merel S et al. State of knowledge and concerns on cyanobacterial blooms and cyanotoxins. 2013 Env International 59:303-327)

**Friday, August 1, 2014****Question:**

Marijuana use can increase heart rate, supine hypertension and postural hypotension. In addition, marijuana smoking has been said to be a trigger for myocardial infarction (MI). What are the characteristics that define the trigger risk for MI following the use of marijuana?

**Answer:**

In order to evaluate if marijuana is a trigger of the onset of an acute MI, the authors of the cited study collected data on marijuana use in 3882 persons who sustained an acute MI. The cited reference reports "the risk of myocardial infarction onset was elevated 4.8 times over baseline (95% confidence interval, 2.4 to 9.5) in the 60 minutes after marijuana use." (Mittleman MA et al. Triggering myocardial infarction by marijuana. 2001 Circulation 103: 2805-2809)

**Thursday, July 31, 2014****Question:**

What is the body part of scorpions known as the telson?

**Answer:**

The telson is the "stinger" of the scorpion located in the animals' tail. The venom glands are located in the telson. (Isbister GK and Bawaskar HS. Scorpion envenomation. 2014 NEJM 371:457-463)

**Wednesday, July 30, 2014****Question:**

What is the primary physiologic mechanism responsible for the phenomenon known as postmortem redistribution with regard to most drugs of abuse?

**Answer:**

According to the cited reference, "Redistributive processes potentially affect the concentration of all drugs of abuse in postmortem cases as a result of diffusion of drug from higher concentration to a lower concentration following disruption of cellular membranes." (Drummer OH. Postmortem toxicology of drugs of abuse. 2004 For Sci Int 142:101-113)

**Tuesday, July 29, 2014****Question:**

Dimethyl formamide (DMF) is used primarily as an industrial solvent in the production of polyurethane products and acrylic fibers. It is also used in the pharmaceutical industry and in the formulation of pesticides and synthetic leathers among other materials. What is the primary toxicity for workers who may be over-exposed to this chemical?

**Answer:**

The primary toxicity associated with industrial DMF exposure is hepatic. The cited reference reported an industrial "outbreak" of liver disease among workers in a factory coating fabric with polyurethane. In this setting, workers used DMF in poorly ventilated areas without appropriate PPE. 62% of workers tested had elevations of either AST or ALT. Enzyme abnormalities occurred almost exclusively in production workers (35 out of 46 abnormal). (Redlich C, et al. Liver disease associated with occupational exposure to the solvent dimethylformamide. 1988 Ann. Intern. Med. 108:680-686)

**Monday, July 28, 2014****Question:**

The Japanese herbal remedy "dai-taiko-so" has been associated with the development of what hepatic disorder? This disorder has also been linked with a variety of viruses including hepatitis C, A and B as well as minocycline, nitrofurantoin, propylthiouracil and the statin drugs?

**Answer:**

Autoimmune hepatitis. (Heneghan MA et al. "Autoimmune hepatitis" 2013 Lancet 382:1433-1444)

**Friday, July 25, 2014**

**Question:**

Rituximab (Rituxan) (RTX) is a biologic agent, B cell depleting antibody, now widely used in a variety of conditions including non-Hodgkin's lymphoma and rheumatoid arthritis. What is the predominate toxicity (organ system) that has been reported in patients taking this agent?

**Answer:**

According to the cited reference, "respiratory events have been reported in up to 38% of patients receiving RTX and include cough, bronchospasm, dyspnea, sinusitis and rhinitis. Likewise respiratory tract infections have been reported in up to 10% of the patients." More serious pulmonary complications reported include bronchiolitis organizing pneumonia, interstitial lung disease and pulmonary fibrosis. (Hadjinicolaou AV et al. Non infectious pulmonary toxicity of rituximab: a systematic review. 2012 Rheumatology

**Thursday, July 24, 2014**

**Question:**

What is the Child-Pugh score and how is this relevant to clinical pharmacology and toxicology?

**Answer:**

The Child-Pugh score provides a general description of the clinical state and severity of patients with hepatic cirrhosis. Five variables are considered: presence of ascites, encephalopathy, serum levels of albumin, total bilirubin, and prolongation of the clotting time. Each of these variables is assigned a score between 1 and 3 according to its level of abnormality. The Child-Pugh score may be found in pharmaceutical manufacturer's literature with regard to indications, contraindications and dose adjustments regarding the use of a drug in patients with liver disease. (Cholongitas E, et al. Systematic review: The model for end-stage liver disease - Should it replace the Child-Pugh's classification for assessing prognosis in cirrhosis? 2005 Aliment Pharmacol Ther. 22(11):1079-89)

**Wednesday, July 23, 2014**

**Question:**

The lionfish is a normal inhabitant of the coral reefs of the Indo-Pacific regions as well as the Red Sea. It is also a frequent addition to home aquariums in the USA. What is the genus and species of the common lionfish? What are the clinical manifestations of lionfish envenomation?

**Answer:**

The lionfish, *Pterois volitans*, has powerful venom that it delivers via dorsal spines. Envenomation from this fish, a member of the Family Scorpaenidae is reported to cause edema and severe local pain at the envenoming site. Systemic effects, including vomiting, fever, diaphoresis and death have all been reported in individuals who have been envenomed by this fish. (Church JE and Hodgson WC. Adrenergic and cholinergic activity contributes to the cardiovascular effects of lionfish (*Pterois volitans*) venom. 2002 Toxicon 40:787-796)

**Tuesday, July 22, 2014**

**Question:**

What is a "NOAEL"?

**Answer:**

NOAEL is the so-called "No-observed-adverse-effect level". According to EPA, the NOAEL is "The highest exposure level at which there are no biologically significant increases in the frequency or severity of adverse effect between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered adverse or precursors of adverse effects." (<http://www.epa.gov/risk/glossary.htm>, accessed June, 2014)

**Monday, July 21, 2014**

**Question:**

What is ChemIDPlus?

**Answer:**

ChemIDPlus is an offering of The National Library of Medicine (NLM). It is a chemical database dictionary of more than 400,000 chemicals that includes names, synonyms, and structures. It also includes links to the NLM and other database resources. ChemIDPlus includes resources that assist users in drawing chemical structures. ([chem.sis.nlm.nih.gov/chemidplus/](http://chem.sis.nlm.nih.gov/chemidplus/); accessed July, 2014)

**Friday, July 18, 2014**

**Question:**

What are the structural differences between dioxins, furans and PCBs?

**Answer:**

Dioxins, furans, and polychlorinated biphenyls (PCBs) are a class of similar chlorinated aromatic organic compounds. Dioxins have two phenyl rings connected by two oxygen atoms. Furans have one or two phenyl rings connected to a furan ring. PCBs have two phenyl rings attached at one point. (<http://www.atsdr.cdc.gov/substances/toxchemicallisting.asp?sysid=29>, accessed June 2014)

**Thursday, July 17, 2014**

**Question:**

What are thought to be the primary constituents of dust generated as a result of the collapse of the World Trade Center buildings following the terrorist attacks of September, 2001?

**Answer:**

A wide variety of materials were reported to have been part of the dust generated. These included man made vitreous fibers, glass fragments, gypsum/anhydrite, phases compatible with concrete, asbestos, metal or metal oxides, and mineral material groups. (<http://pubs.usgs.gov/of/2005/1165/508OF05-1165.html#heading07>) The reference cited below reports: "Although sampling and analysis of the WTC dust was delayed and limited, it is widely accepted that it was hazardous containing a large amount of respirable particles, a high concentration of polyaromatic hydrocarbons, and, most notably, a very caustic pH (9.5-11) (Lioy PJ et al. Characterization of the dust/smoke aerosol that settled east of the World Trade Center in lower Manhattan after the collapse of the WTC 11 September 2001. 2001 Env Health Perspect 110: 703-714 as cited in de la Hoz R et al. Occupational toxicant inhalation injury: the World Trade Center experience. 2008 Int Arch Occup Environ Health

**Wednesday, July 16, 2014**

**Question:**

What are the risk factors for the development of bleomycin-induced pulmonary toxicity?

**Answer:**

The cited reference reports: "The risk of developing bleomycin-induced pulmonary toxicity is increased by a number of factors, including increasing age, higher doses of the drug, impaired renal function (creatinine clearance <35 ml/min), high concentration oxygen therapy and radiation therapy to the thorax. There are conflicting data as to whether concomitant granulocyte colony stimulating factor (G-CSF) therapy increases the risk of bleomycin-induced lung injury." (Fyfe AJ and McKay P. Toxicities associated with bleomycin. 2010 J R Coll Physicians Edinb 40:213-215)

**Tuesday, July 15, 2014**

**Question:**

2-Butanone is a chemical manufactured in large quantities. Nearly half of its use is in paints and other coatings because it will quickly evaporate into the air and it dissolves many substances. It is also used in glues and as a cleaning agent. 2-Butanone also occurs as a natural product. It is made by some trees and found in some fruits and vegetables in small amounts. It is also released to the air from car and truck exhausts. What is the more common name for 2-butanone?

**Answer:**

Methyl ethyl ketone is the more commonly used name for 2-butanone. (<http://www.atsdr.cdc.gov/toxfaqs/tf.asp?id=342&tid=60>; accessed June ,2014)

**Monday, July 14, 2014**

**Question:**

Epidural injections of methylprednisolone acetate have been linked to outbreaks of meningitis caused by which mold organism?

**Answer:**

Exserohilum rostratum. (McCarthy M et al. Mold infections of the central nervous system. 2014 NEJM 371(2):150-160)

**Friday, July 11, 2014**

**Question:**

What is the primary habitat of the blue-ringed octopus (*Hapalochlaena* sp)?

**Answer:**

According to the cited reference, "*Hapalochlaena* sp. lives in rock pools in seas around Australia, the Indian subcontinent, the Indo-pacific region and Japan." (Cavazzoni E et al. Blue-ringed octopus (*Hapalochlaena* sp) envenomation of a 4-year old boy: A case report. 2008 Clin Tox 46(8):760-761)

**Thursday, July 10, 2014**

**Question:**

Optic neuropathy is a recognized complication of treatment with the drug ethambutol. What are the clinical manifestations of this complication of ethambutol therapy? What are the risk factors associated with the development of ethambutol related optic neuropathy?

**Answer:**

The optic neuropathy associated with ethambutol therapy usually involves decreased visual acuity, central scotomas and deficits in color vision. Increasing age, duration of ethambutol therapy, inappropriate dosing and co-existing renal disease (ethambutol is renal cleared) are the usual risk factors associated with the development of ethambutol related optic neuropathy. (Estlin KA and Sadun AA. Risk factors for ethambutol optic toxicity. 2010 Int Ophthalmol 30:63-72)

**Wednesday, July 9, 2014**

**Question:**

During the 2006–2007 time frame, an epidemic of severe contact dermatitis cases related to newly acquired sofas and chairs manufactured in China were reported. Buttocks, back, thighs, or arms were the initial locations of this severe dermatitis. What was determined to be the cause for this outbreak of dermatitis?

**Answer:**

The cause for the so-called "Chinese sofa/chair dermatitis" epidemic was probably a contact allergy to the chemical dimethylfumarate (DMF), a potent contact sensitizer added to fabric as a mold inhibitor and biocide. (Rantanen T. The cause of Chinese sofa/chair dermatitis epidemic is likely to be contact allergy to dimethylfumarate, a novel potent contact sensitizer. 2008 Br J Dermatol 159: 218–221)

**Tuesday, July 8, 2014**

**Question:**

A history of epilepsy not treated with antiepileptic drugs (AEDs) in pregnancy does not increase the risk for birth defects. However drug specific risks in pregnancy for valproic acid and carbamazepine have been reported. What are the specific birth defects reportedly associated with the use of these drugs in pregnancy?

**Answer:**

According to the cited reference, "Drug-specific increased risks were observed for valproic acid in relation to neural tube defects [adjusted odds ratio (aOR), 9.7; 95% confidence interval (CI), 3.4–27.5], oral clefts (aOR, 4.4; 95% CI, 1.6–12.2), heart defects (aOR, 2.0; 95% CI, 0.78–5.3), and hypospadias (aOR, 2.4; 95% CI, 0.62–9.0), and for carbamazepine in relation to neural tube defects (aOR, 5.0; 95% CI, 1.9–12.7) after controlling for folate use. Epilepsy history without AED use did not seem to increase risk." (Werler MM et al. Use of antiepileptic medications in pregnancy in relation to risks of birth defects. 2011 Ann Epidemiol 21:842-850)

**Monday, July 7, 2014**

**Question:**

Up to 2% of renal stones may be induced by medications. Some medications may induce renal stones because of their high urinary excretion and relatively poor solubility with resultant crystallization in urine. Which drugs have been associated with the production of renal stones via this mechanism?

**Answer:**

Medicines that may induce the production of renal stones in the manner referred to in the question include triamterene, sulfonamides, quinolone antibiotics, guaifenesin, ephedrine, pseudoephedrine, and indinavir. (Small E and Sandefur BJ. Acute renal failure after ingestion of guaifenesin and dextromethorphan. 2014 J Emerg Med 47(1): 26-29)

**Friday, July 4, 2014****Question:**

What treatment modality may be considered in cases of glyphosate ingestion that may be associated with poor prognostic factors (e.g. advanced age, large volume ingested, and impaired consciousness) as well as severe acidosis and renal injury?

**Answer:**

A recent report detailed a 62-year-old man brought to the emergency department 8.5 hours after drinking a bottle of commercial herbicide containing a 41% solution of glyphosate isopropylamine, in polyoxyethyleneamine (POEA) surfactant and water. The authors reported "the successful clearance of glyphosate using hemodialysis, with corresponding clinical improvement." These authors further reported "The extraction ratio and hemodialysis clearance (for glyphosate) were calculated to be 91.8% and 97.5 mL/min, respectively. (Garlich FM et al. Hemodialysis clearance of glyphosate following a life-threatening ingestion of glyphosate surfactant herbicide. 2014 Clin Tox 52:66-71)

**Thursday, July 3, 2014****Question:**

What are so-called "metal working fluids" (MWFs), how widespread is the problem of exposure to these substances and what clinical effects result from exposure to MWFs?

**Answer:**

MWFs reduce heat and friction and help remove metal particles in industrial machining and grinding operations. Formulations, range from straight oils (e.g. petroleum oils) to water-based fluids, which include soluble oils and semisynthetic/synthetic fluids as well as complex mixtures of oils, emulsifiers, anti-weld agents, corrosion inhibitors, extreme pressure additives, buffers (alkaline reserve), biocides, and other additives.

Some 1.2 million workers in machine finishing, machine tooling, and other metalworking and metal-forming operations may be potentially exposed via both the dermal and inhalational routes.

Occupational exposures to metalworking fluids may cause a variety of health effects including hypersensitivity pneumonitis (HP), chronic bronchitis, impaired lung function, and asthma. Dermatologic exposures are most commonly associated with allergic and irritant dermatitis. (<http://www.cdc.gov/niosh/topics/metalworking>. Accessed June, 2014)

**Wednesday, July 2, 2014****Question:**

Guarana is a common additive found in a variety of so-called energy drinks. What is guarana?

**Answer:**

The cited reference reports "Guarana, also known as Brazilian cocoa, is a South American plant that is commonly added to energy drinks. It contains a substance called guaranine, which is caffeine, with 1 g of guarana being equivalent to as much as 40 mg of caffeine." The authors go on to note "...when an energy drink lists its caffeine content, it is usually not taking into account the guarana, which has been reported to exert a more prolonged effect than an equivalent amount of caffeine. In reality, when a drink is said to contain caffeine plus guarana, it contains caffeine plus more caffeine. Guayana has not been evaluated by the FDA for safety, effectiveness, or purity." (Blankson KL et al. Energy drinks: What teenagers (and their doctors) should know. 2013 Pediatrics in Review 34(2):55-62)

**Tuesday, July 1, 2014****Question:**

What is the National Toxicology Program "Report on Carcinogens"?

**Answer:**

The Report on Carcinogens (RoC) is a congressionally mandated, science-based, public health report that identifies agents, substances, mixtures, or exposures (collectively called "substances") in our environment that may potentially put people in the United States at increased risk for cancer.

The National Toxicology Program (NTP) prepares the RoC on behalf of the Secretary, Health and Human Services.

Published biennially, each edition of the report is cumulative and consists of substances newly reviewed in addition to those listed in previous editions. The 12th RoC, the latest edition, was published on June 10, 2011. The 13th RoC is under development.

For each listed substance, the RoC contains a substance profile which provides information on:

1- Cancer studies that support the listing—including those in humans, animals and on possible mechanisms of action

2- Potential sources of exposure to humans

3- Current Federal regulations to limit exposures (<http://ntp.niehs.nih.gov/?objectid=03C9B512-ACF8-C1F3-ADBA53CAE848F635>. Accessed June, 2014)

**Monday, June 30, 2014****Question:**

What is the "OIICS"?

**Answer:**

The Occupational Injury and Illness Classification System (OIICS) was developed by the Bureau of Labor Statistics (BLS) to provide a standardized coding system for characterizing work-related injuries and illnesses. The OIICS has four component hierarchical coding structures or "code trees." Each structure is used to characterize specific incident concepts (referred to here as coding components). Two coding structures are used to describe the characteristics of the injury or illness (i.e., "Nature" and "Part of Body Affected") and two structures are used to describe the incident circumstances (i.e., "Source/Secondary Source of injury or illness", and "Event or Exposure"). The Source and Secondary Source coding components utilize the same hierarchical coding structure. However, the coding rules differ slightly. Thus, the four coding structures represent five data elements or conceptual components.

(<http://www.cdc.gov/wisards/oics/About.aspx>. Accessed June, 2014)

**Friday, June 27, 2014**

**Question:**

Selective serotonin reuptake inhibitors (SSRIs) are noted to be generally safe from the point of view of cardiovascular toxicity. However, one SSRI has been reported to be associated with the development of acute heart failure in the overdose situation. Which SSRI has been reported to be associated with the development of acute heart failure in the overdose setting?

**Answer:**

The authors of the cited article note that hypertension and tachycardia may be observed following "moderate venlafaxine exposure". They further note an association between venlafaxine overdose and the development of acute congestive heart failure. The authors indicate that the underlying mechanism for heart failure in this setting has yet to be elucidated. (Batista M et al. The spectrum of acute heart failure after venlafaxine overdose. 2013 Clin Tox 51:92-95)

**Thursday, June 26, 2014**

**Question:**

When the DRESS syndrome is accompanied by exfoliative dermatitis in what setting are patients best managed?

**Answer:**

The cited reference notes that DRESS (drug reaction with eosinophilia and systemic symptoms) syndrome complicated by exfoliative dermatitis is best managed in an intensive care setting or a burn unit. (Husain Z et al. DRESS syndrome. Part II. Management and therapeutics. 2013 J Am Acad Dermatol 68: 709.e1-9)

**Wednesday, June 25, 2014**

**Question:**

What is the prevalence rate of use of antidepressant medication during pregnancy in the United States and what group of anti-depressants are the most commonly prescribed antidepressants during pregnancy?

**Answer:**

According to the cited reference, the prevalence rate of use of antidepressant medication during pregnancy in the United States ranges from 8 to 13% and "Selective serotonin reuptake inhibitors (SSRIs) are the most commonly prescribed antidepressants during pregnancy." (Huybrechts KF et al. Antidepressant use in pregnancy and the risk of cardiac defects. 2014 NEJM 370(25): 2397-2407)

**Monday, June 23, 2014**

**Question:**

Ivermectin (22,23-dihydroavermectin B<sub>1a</sub> + 22,23-dihydroavermectin B<sub>1b</sub>) is an orally administered semisynthetic macrocyclic lactone antibiotic used to treat scabies as well as a variety of worm and filarial infestations in both humans and animals. Occasionally treatment is associated with fever, malaise, myalgias and postural hypotension. What is the etiology of these adverse reactions when ivermectin is used to treat scabies and other parasitic infections?

**Answer:**

The cited reference notes that "These adverse reactions are probably related to the intensity of the intensity of the filarial infection and the release of parasitic antigens" as opposed to an adverse effect of the drug itself. (Currie BJ and McCarthy JS. Permethrin and ivermectin for scabies. 2010 NEJM 362:717-725)

**Friday, June 20, 2014**

**Question:**

What potentially harmful exposure may be associated with the breakage of CFL's?

**Answer:**

CFLs are "compact fluorescent lamps". These light bulbs were introduced in the US with the intention of reducing domestic energy consumption. The cited reference notes that "an important disadvantage of fluorescent lamps is that CFLs contain milligram quantities of mercury." The authors go on to report that according to one recent study, "once a CFL breakage event occurs, mercury vapor, liquid mercury (if present) and mercury adsorbed onto the phosphorous powder is released." They further report that after a CFL breaks, indoor [mercury] air concentrations could potentially exceed regulatory thresholds of concern. (Sarigiannis DA et al. Exposure analysis of accidental release of mercury from compact fluorescent lamps (CFLs) 2012 Sci Tot Environ 435-436:306-315)

**Thursday, June 19, 2014**

**Question:**

What is the occupational medicine significance of the so-called Triangle Shirtwaist Factory fire (March 25,1911)?

**Answer:**

The Triangle Shirtwaist Factory fire (occurred in Manhattan, New York City), one of the nation's most deadly and horrific, led to some of the nation's strongest changes in worker safety in the manufacturing industry. New York City and New York State, over the next few years, adopted the country's strongest worker safety protection laws. Initially addressing fire safety, these laws eventually became model legislation for the rest of the country and state after stated enacted much more strict worker safety laws. (<http://www.dol.gov/shirtwaist/aftermath.htm>; accessed June, 2014)

**Wednesday, June 18, 2014**

**Question:**

What is Naloxegol?

**Answer:**

Naloxegol is an oral, peripherally acting, mu-opioid receptor antagonist used for the treatment of opioid-induced constipation. (Chey WD, et al. Naloxegol for opioid-induced constipation in patients with non-cancer pain. 2014 NEJM published online (DOI: 10.1056/NEJMoa1310246)

**Tuesday, June 17, 2014**

**Question:**

The FDA has recently ordered the manufacturer of eszopiclone (Lunesta) to lower the recommended starting dose of this drug for both men and woman. What was the rationale for this action on the part of the FDA?



**Answer:**

Eszopiclone (Lunesta) is a benzodiazepine receptor agonist used to treat insomnia. The cited reference notes that an evening dose of 3 mg of this drug “can impair driving skills, memory and coordination for more than 11 hours.” Consequently, the FDA has required the evening dose of this drug be lowered to 1 mg. The cited article points out that the elimination half-life for eszopiclone is longer than that of any other drug in the same class, zolpidem (Ambien and generics) as well as zaleplon (Sonata and generics). (The Medical Letter, June 9, 2014, 56(1444): 48)

**Monday, June 16, 2014****Question:**

What toxin is causative of “bitter bottle gourd toxicity”? What is the clinical syndrome caused by this poisoning?

**Answer:**

Bottle gourds are plants included in the Family Cucurbitaceae. These plants, especially when over-ripe, contain the substance cucurbitacin. Cucurbitacins are triterpenoids and, if ingested, reportedly increase capillary permeability causing severe capillary leak syndrome leading to hypotension. The authors of the cited article report that bottle gourds are usually consumed in South Asian countries and may be included with some Ayurvedic medicines. The ingestion of bottle gourds containing high concentrations of cucurbitacins, may result in severe GI effects within 60 minutes of ingestion. These effects include diarrhea, vomiting, GI bleeding and hypotension. Several outbreaks of cucurbitacin poisoning have been reported including a 1984 California outbreak of over 200 cases attributed to ingestion of bitter zucchini. (Ho CH et al. Bitter bottle gourd (Lagenaria siceraria) toxicity. 2014 J Emerg Med 46(6): 772-775)

**Friday, June 13, 2014****Question:**

Exposure to paralytic shellfish toxins (PSTs) may result in the severe and occasionally fatal illness known as paralytic shellfish poisoning (PSP), also known as saxitoxin pufferfish poisoning (SPFP). What is the mechanism causing these maladies and what is the potential public health impact of these diseases?

**Answer:**

The cited reference notes that PSP is “caused when PSTs reversibly bind voltage-gated Na<sup>+</sup> channels in an equimolar ratio. This is mediated by the interaction between the positively charged guanidinium groups of saxitoxin with negatively charged carboxyl groups at site 1 of the Na<sup>+</sup> channel, thereby blocking the pore.” The authors further posit out that “The threat of PSP is not only a major cause of concern for public health but is also detrimental to the economy. Outbreaks of PSTs often result in the death of marine life and livestock, the closure of contaminated fisheries, while the continual expenditure required for the maintenance and running of monitoring programs, all combine to present a major economic burden around the world.” (Weise M et al. Neurotoxic alkaloids: Saxitoxin and its analogs. 2010 Marine Drugs 8:2085-2211)

**Thursday, June 12, 2014****Question:**

What is the utility of the serum lactate level in the diagnosis of cyanide poisoning?

**Answer:**

According to the cited reference, cyanide intoxication should be suspected in “Fire accident patients where arterial blood sampling reveal metabolic acidosis with a lactate above 8 mmol/l, as the concentration of lactate increases proportional with the rate of CN poisoning. A lactate of 10 mmol/l is a sensitive and specific indicator of CN intoxication.” (Baud FJ: Cyanide: critical issues in diagnosis and treatment. Hum Exp Toxicol 2007, 26:191-201 as cited in Lawson-Smith P, et al. Cyanide intoxication as part of smoke inhalation- a review on diagnosis and treatment from the emergency perspective. 2011 Scand J Trauma Resusc and Emerg Med 19:14)

**Wednesday, June 11, 2014****Question:**

Soman (3,3-dimethylbutan-2-yl methylphosphonofluoridate) has a highly branched alkoxyl group and is one of the most lethal nerve agents with a very short aging half-life. What is the approximate aging half-life of soman?

**Answer:**

The aging half-life of soman ranges from 1.87 minutes to 4.62 minutes. (Sirin GS et al. Aging mechanisms of soman inhibited acetylcholinesterase. 2012 J Phys Chem. 116:12199-12207)

**Tuesday, June 10, 2014****Question:**

Recurrent pericarditis is an important complication of pericarditis. While various anti-inflammatory agents are used for treatment (i.e., acetylsalicylic acid, indomethacin, steroids, and colchicine), only colchicine has been proven to be efficacious for prevention. What is the most commonly reported side effect of colchicine that is associated with cessation of therapy in patients being treated for pericarditis with colchicine?

**Answer:**

According to the cited reference, “The most common reported side effect is gastrointestinal intolerance that was associated with cessation of therapy”. (Imazio M et al. Efficacy and safety of colchicine for pericarditis prevention. Systematic review and meta-analysis. 2012 Heart 98:1078-1082)

**Monday, June 9, 2014****Question:**

What is the addictive potential of marijuana use?

**Answer:**

According to the cited article “Despite some contentious discussions regarding the addictiveness of marijuana, the evidence clearly indicates that long-term marijuana use can lead to addiction. Indeed, approximately 9% of those who experiment with marijuana will become addicted (according to the criteria for dependence in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition [DSM-IV]). The number goes up to about 1 in 6 among those who start using marijuana as teenagers and to 25 to 50% among those who smoke marijuana daily.” (Hall W and Degenhardt L. Adverse health effects of non-medical cannabis use. Lancet 2009; 374:1383-91 as cited in Volkow ND et al. Adverse health effects of marijuana use. 2013 NEJM 370(23): 220-227)

**Thursday, June 5, 2014**

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**Question:**

What are the symptoms commonly associated with a sting inflicted by the Weever fish? What is the composition of the venom injected by this fish?

**Answer:**

The cited reference reports "The symptoms mostly commonly arising from a Weever fish sting are: severe pain, local erythema and oedema. Systemic symptoms may sometimes occur: headache, syncope, bradycardia, fever and hypotension." Continuous joint pain and severe fatigue following a Weever sting have also been reported. The venom's composition has yet to be completely elucidated however it is known that Weever fish venom contains a mixture of biogenic amines including 5-hydroxytryptamine, epinephrine, norepinephrine and histamine. (Dekker CJ. Chronic pain and impairment of function after a sting by the great weever fish (*Trachinus draco*). [Abstract] *Nederlands Tijdschrift voor Geneeskunde*. 145(18): 881-4, 2001 May 5.)

**Wednesday, June 4, 2014**

**Question:**

What is the preferred antitoxin for adult botulism?

**Answer:**

The preferred antitoxin for adult botulism is the equine heptavalent antitoxin. This is a new antitoxin that includes antibodies against all seven botulinum neurotypes (A through G). This antitoxin is available through state and local health departments via the CDC. (The Medical Letter May 26, 2014, 56(1443):44)

**Tuesday, June 3, 2014**

**Question:**

What is the composition of the product known as "Corian" used in the manufacture of kitchen and bathroom counters and some shower wall units?

**Answer:**

Corian is the trade name for a product described in the cited reference as "a solid-surface material composed of acrylic polymer and aluminum trihydrate". (Raghu G., et al. Pulmonary fibrosis associated with aluminum trihydrate (Corian) dust. 2014 *NEJM* 370:2154-2156)

**Monday, June 2, 2014**

**Question:**

The Russell's viper is responsible for 30–40% of the snake bites, and to the most number of severe envenoming and fatalities compared to other snakes in Sri Lanka. What are the clinical characteristics associated with envenoming by this snake?

**Answer:**

According to the cited reference, "Coagulopathy and acute kidney injury [are] the major life threatening systemic manifestations of bites by this snake in Sri Lanka. Neuro-muscular paralysis, characterized by ophthalmoplegia and ptosis, have been commonly observed in these with rare occurrence of respiratory muscle paralysis. Rhabdomyolysis, chronic renal failure, myocardial infarction and secondary hypopituitarism have also been reported in Russell's viper bite patients in Sri Lanka. Although generally not severe, local swelling has been a common feature..." (Kularatne SAM, Silva A, Weerakoon K, Maduwage K, Walathara C, et al. (2014) Revisiting Russell's Viper (*Daboia russelii*) Bite in Sri Lanka: Is Abdominal Pain an Early Feature of Systemic Envenoming? *PLoS ONE* 9(2): e90198. doi:10.1371/journal.pone.0090198)

**Friday, May 30, 2014**

**Question:**

Dermal exposure to sulfur mustard characteristically is associated with a latent period of 2-24 hours prior to the development of symptoms. In the evaluation of an individual with a sulfur mustard skin exposure what is the significance of the complaint of immediate (as opposed to delayed) burning sensation of the skin?

**Answer:**

In some instances the agent Lewisite (an arsenic containing vesicant-inducing material) is added to sulfur mustard in order to decrease the freezing point of the sulfur mustard thereby rendering it more effective in environments with colder temperatures. Immediate skin burning on contact with sulfur mustard often signifies that Lewisite has been combined with the sulfur mustard. In these cases it may be reasonable to perform urine assays for Lewisite in addition to rendering care for the sulfur mustard exposure. (Weibrecht K et al. Sulfur mustard exposure presenting to a community emergency department. 2012 *Ann Emerg Med* 59:70-74)

**Thursday, May 29, 2014**

**Question:**

Currently available cyanide antidotes require the administration of one or more drugs via the intravenous route. What are the obstacles to the development of a cyanide antidote that might be amenable to administration via the intra-muscular (IM) route?

**Answer:**

According to the cited reference, "The IM mode for cyanide antidote administration poses a technical challenge in that (a) large doses must be administered within a short time for maximal efficacy; (b) inflammatory responses must be minimal at the IM injection site; hence, biocompatibility is of prime consideration; and (c) the antidote must be highly water-soluble as a consequence of (a). If an anti-cyanide agent fulfilling the above criteria can be prepared and developed, treatment of mass casualty cyanide victims could become reality, especially if mechanical injection devices presently available commercially, or adapted for this use, can be implemented." (Patterson SE et al. Cyanide antidotes for mass casualties: Water-soluble salts of the dithiane (sulfanegen) from 3-mercaptopyruvate for intramuscular administration. 2013 *J Med Chem* 56(3): 1346-1349)

**Wednesday, May 28, 2014**

**Question:**

In December 1983, more than 3,000 gallons of a chemical were discharged from a partially below-ground storage tank at the EC Electroplating company in Garfield, New Jersey. As a result, ground water near the EC Electroplating site has been contaminated with this chemical. During heavy rains, flooding may occur in the basements of some Garfield homes and businesses. When the water recedes, the residue dries out and leaves a yellow dust that can pose a health risk to persons living in or using these properties. What is the chemical at issue in this situation?

**Answer:**

The chemical released in this incident was a chromium based plating solution. In late summer 2010, EPA alerted ATSDR and New Jersey DHSS that data showed very high levels of hexavalent chromium in the basement of a Garfield property. ([http://www.atsdr.cdc.gov/sites/ec\\_electroplating/](http://www.atsdr.cdc.gov/sites/ec_electroplating/), accessed April, 2014)

**Tuesday, May 27, 2014****Question:**

What is the so-called “CFR Title 49, Part 40”?

**Answer:**

The Code of Federal Regulations (CFR) annual edition is the codification of the general and permanent rules published in the Federal Register by the departments and agencies of the Federal Government. Title 49, Part 40 specifically defines “procedures for transportation workplace drug and alcohol testing programs” ([http://www.dot.gov/sites/dot.dev/files/docs/PART40\\_2012.pdf](http://www.dot.gov/sites/dot.dev/files/docs/PART40_2012.pdf), accessed May, 2014)

**Monday, May 26, 2014****Question:**

Fomepizole (4-methylpyrazole) was approved in the United States for the treatment of ethylene glycol poisoning in 1997 and in 2000 for the treatment of methanol toxicity. What is the mechanism of action of this antidote?

**Answer:**

The cited reference notes that fomepizole (4-methylpyrazole) is a competitive inhibitor of alcohol dehydrogenase that prevents the formation of metabolites of ethylene glycol and methanol. (Brent J. Fomepizole for ethylene glycol and methanol poisoning. 2009 NEJM 360: 2216-2223)

**Friday, May 23, 2014****Question:**

What is the EPA Toxics Release Inventory?

**Answer:**

The Toxics Release Inventory (TRI) tracks the management of over 650 toxic chemicals that pose a threat to human health and the environment. U.S. facilities in certain industry sectors that manufacture, process, or otherwise use these chemicals in amounts above established levels must report how each chemical is managed through recycling, energy recovery, treatment, and releases to the environment. A “release” of a chemical means that it is emitted to the air or water, or placed in some type of land disposal. The information submitted by facilities to the EPA and states is compiled annually as the Toxics Release Inventory or TRI, and is stored in a publicly accessible database in Envirofacts. (<http://www.epa.gov/enviro/facts/tri/>, accessed May, 2014)

**Thursday, May 22, 2014****Question:**

DEET is a chemical (N,N-diethyl-meta-toluamide) used as the active ingredient in many insect repellent products. DEET was developed by the U.S. Army in 1946 and was registered for use by the general public in 1957. DEET containing products are currently available in a variety of forms: liquids, lotions, sprays, and even impregnated materials, such as wristbands. What concentration of DEET may be found in products approved for application to human skin?

**Answer:**

DEET formulations registered for direct application to human skin contain from 4% to 100% DEET. (<http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=201>, accessed April, 2014)

**Wednesday, May 21, 2014****Question:**

Gasoline is a complex mixture of hydrocarbons and additives and contains roughly 60% to 70% alkanes, 25% to 30% aromatics, and 6% to 9% alkenes. What is the primary cause of morbidity and mortality associated with the ingestion of gasoline?

**Answer:**

The primary cause of morbidity and mortality associated with the ingestion of gasoline is related to pulmonary aspiration. (Rahman I., et al. Gasoline ingestion: A rare cause of pancytopenia. 2009 Am J Med Sci 338(5): 433-434)

**Tuesday, May 20, 2014****Question:**

What is arsine oil?

**Answer:**

Arsine oil is a mixed arsenical agent produced by Nazi Germany during the WW II. Arsine oil contained A) 50% phenyldichloroarsine B) 35% diphenylchloroarsine C) 5% arsenic trichloride and D) 5% triphenylarsine. (Matousek J. Health and environmental threats associated with the destruction of chemical weapons. 2006 Ann NY Acad Sci 1076:549-558)

**Monday, May 19, 2014****Question:**

What are the four arsenic containing chemical warfare agents?

**Answer:**

The four arsenic-containing chemical warfare agents are Adamsite (technical, 10-chloro-9-10-dihydrophenarsazine), Clark 1 (Diphenyl arsine chloride), Clark 2 (Diphenyl arsine cyanide), and Lewisite (2-chloro-ethenyl dichloro arsine)(Henriksson J et al. The toxicity of organoarsenic-based warfare agents: In vitro and in vivo studies. 1996 Arch Environ Contam Toxicol 30:213-219)

**Friday, May 16, 2014**

**Question:**

On March 26, 2012, the U.S. Occupational Safety and Health Administration (OSHA) adopted the United Nations Globally Harmonized System (GHS). What is the GHS?

**Answer:**

GHS is an international initiative to develop a uniform approach to hazard communication that would apply across international borders. GHS was negotiated via a multi-year process by hazard communication experts from a variety of different countries. GHS employs separate and distinct criteria and methodology for hazard classification and categorization of chemical substances. (Hofert JM et al. GHS adoption in the face of Daubert. 2014 Occupational Health and Safety 83(5): 47-52)

**Thursday, May 15, 2014**

**Question:**

What substance, noted to be an important recreational drug and public health problem in the late 1990's and early 2000's, once found limited use as an anesthetic agent as well as in the treatment of narcolepsy and alcoholism?

**Answer:**

Gamma hydroxybutyric acid (GHB), previously a popular substance of abuse, once found limited use as an anesthetic agent as well as in the treatment of narcolepsy and alcoholism. (Snead O and Gibson KM. Gamma hydroxybutyric acid. 2005 NEJM 352:2721-2732)

**Wednesday, May 14, 2014**

**Question:**

What is the suggested duration of venom immunotherapy used for hymenoptera sting hypersensitivity?

**Answer:**

The authors of the cited article report that "The duration of venom immunotherapy should be at least 3 to 5 years." (Casale TB and Burks AW. Hymenoptera-sting hypersensitivity. 2014 NEJM 370:1432-1439)

**Tuesday, May 13, 2014**

**Question:**

Methimazole and propylthiouracil (PTU) are the two most commonly prescribed antithyroid drugs. Both drugs have been reported to cause life-threatening agranulocytosis. What is the incidence of this serious drug reaction and what are the common clinical presenting features for agranulocytosis due to methimazole or PTU?

**Answer:**

According to the cited reference, "the incidence of agranulocytosis is 0.37% with propylthiouracil and 0.35% with methimazole." Mortality secondary to anti-thyroid drug-induced agranulocytosis has been reported to be as high as 21.5%. The authors further state "Clinical features are usually abrupt in onset with fever or sore throat as common presenting complaints." (Khaliq W et al. Agranulocytosis secondary to propylthiouracil. 2012 Q J Med 105(11): 1109-1111)

**Monday, May 12, 2014**

**Question:**

Progressive multifocal leukoencephalopathy (PML) is a demyelinating central nervous system condition known to be caused by the JC virus (JVC). PML has also been reported as an adverse event associated with what drug used in the treatment of patients with multiple sclerosis?

**Answer:**

The cited reference reports that PML is "a feared adverse event associated with natalizumab treatment in patients with multiple sclerosis." (Boster AL et al. Lessons learned from fatal progressive multifocal leukoencephalopathy in a patient with multiple sclerosis treated with natalizumab. JAMA Neurol. 2013; 70(3): 398-402)

**Friday, May 9, 2014**

**Question:**

What are the clinical characteristics of envenomed bites of the Gaboon viper (*Bitis gabonica*) and what is the recommended treatment for these bites?

**Answer:**

The cited reference notes that the usual symptoms associated with envenomation caused by *Bitis gabonica* include "rapid onset swelling of the bite area, later becoming very painful, bleeding and hemorrhagic edema at the bite site and finally, dyspnea and loss of consciousness with hematuria, hematemesis and local tissue necrosis." The treatment of choice for the envenomation by this snake is the timely administration of appropriate antivenom. (Marsh N et al. Gaboon viper (*bitis gabonica*) envenomation resulting from captive specimens- A review of five cases. 2007 Clin Tox 45(1):60-64)

**Thursday, May 8, 2014**

**Question:**

What is epichlorohydrin (ECH) and what is posited to be the predominant mechanism of toxicity for this chemical?

**Answer:**

Epichlorohydrin is a bifunctional alkylating agent that is widely used in the production of epoxy resins, glycerine, elastomers and a variety of specialty chemicals. ECH has been classified as a "probable human carcinogen". It is believed that more than 250,000 US workers may have the potential for exposure to this chemical in the course of their work. The mechanism of toxicity for ECH probably involves its potential to form DNA cross-links between deoxyguanosine residues possibly leading to important chromosomal aberrations in some cases. (Romano KP et al. DNA interstrand cross-linking by epichlorohydrin. 2007 Chem Res Toxicol 20:832-838)

**Wednesday, May 7, 2014**

**Question:**

The US EPA defines and promulgates a number of regulatory standards for drinking water. What is the so-called MCL for drinking water as defined by EPA?

**Answer:**

The "MCL" is the "Maximum Contaminant Level". The MCL is defined as "The highest level of a contaminant that is allowed in drinking water. MCLs are set as close to MCLGs (Maximum Contaminant Level Goals) as feasible using the best available treatment technology and taking cost into consideration. MCLs are enforceable standards." (<http://water.epa.gov/drink/contaminants/index.cfm#SecondaryList>), accessed April 2014)

**Tuesday, May 6, 2014**

**Question:**

What is diisopropyl methylphosphonate?

**Answer:**

Diisopropyl methylphosphonate, also known as DIMP, diisopropyl methane-phosphonate, phosphonic acid, and methyl-bis-(1-methylethyl)ester is a chemical by-product resulting from the manufacture of Sarin (GB), a well-known chemical nerve agent. A chemical by-product is a chemical that is formed while making another substance. Sarin was produced and stored only in the Rocky Mountain Arsenal outside of Denver, Colorado. Production of Sarin in the United States was discontinued in 1957. Diisopropyl methylphosphonate is not known to occur naturally in the environment. It is not likely to be produced in the United States in the future because of the signing of a chemical treaty that bans the use, production, and stockpiling of poison gases. Diisopropyl methylphosphonate is a colorless liquid. (<http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=203>, accessed April, 2014)

**Monday, May 5, 2014**

**Question:**

What is the usual dose of methylene blue for the treatment of methemoglobinemia and what are the adverse effects of this drug that may occur when administered at doses in excess of the recommended dose?

**Answer:**

According to the cited reference, the "Dosing for methylene blue for methemoglobinemia is typically 1-2 mg/kg of a 1% solution intravenously." The authors go on to state: "At higher doses (5-7 mg/Kg), EKG abnormalities (T wave inversion, diminished R waves), shortness of breath, chest discomfort, nausea, diarrhea, diaphoresis and abdominal discomfort have been reported. Similarly at doses > 4 mg/Kg, reversible skin, feces, and urine discoloration occurs. Paradoxically, at doses between 4 and 15 mg/Kg, methylene blue may cause methemoglobinemia." (Lo J, et al. A review of methylene blue treatment for cardiovascular collapse. 2014 J Emerg Med 46(5):670-679)

**Friday, May 2, 2014**

**Question:**

The so-called "non-24 hour sleep-wake disorder" is a common problem for people who are totally blind. FDA has recently approved the drug tasimelteon for the treatment of this disorder. What is the mechanism of action of this drug?

**Answer:**

Tasimelteon is a melatonin receptor agonist. (The Medical Letter, April 26, 2014, 56(1441): 34-35)

**Thursday, May 1, 2014**

**Question:**

Is the administration of multiple vaccines in children, in a simultaneous manner, considered to be safe practice?

**Answer:**

The Centers for Disease Control and Prevention state: "The available scientific data show that simultaneous vaccination with multiple vaccines has no adverse effect on the normal childhood immune system. A number of studies have been conducted to examine the effects of giving various combinations of vaccines simultaneously. These studies have shown that the recommended vaccines are as effective in combination as they are individually, and that such combinations carry no greater risk for adverse side effects. Consequently, both the Advisory Committee on Immunization Practices and the American Academy of Pediatrics recommend simultaneous administration of all routine childhood vaccines when appropriate. Research is underway to find methods to combine more antigens in a single vaccine injection (for example, MMR and chickenpox)." (<http://www.cdc.gov/vaccinesafety/vaccines/multiplevaccines.html>, accessed April, 2014)

**Wednesday, April 30, 2014**

**Question:**

What is aldicarb?

**Answer:**

Aldicarb (propanal, 2-methyl-2-(methylthio)-O-[(methyl-amino) carbonyl] oxime) is a carbamate insecticide and nematocide marketed under the brand name Temik. As a carbamate, aldicarb is a potent but reversible cholinesterase inhibitor. (Proenca P et al. Aldicarb poisoning: one case report. 2004 For Sci Int 146S: S79-S81)

**Tuesday, April 29, 2014**

**Question:**

Energy drinks have become extremely popular in the US culture today. Some of these drinks may contain high concentrations of caffeine as well as other substances including taurine, kola nut, Ginkgo biloba, Ginseng, milk thistle, 1,3 dimethylamylamine, guarana and yerba mate, among others. Energy drinks have been implicated as causative of cardiac ischemic in some cases. What mechanisms have been proposed for the development of cardiac ischemia that may be attributed to the excessive use of energy drinks?

**Answer:**

The cited reference notes a variety of potential mechanisms for the development of cardiac ischemia in those who heavily use or abuse some energy drinks. These include a possible increase in platelet aggregation, decreased myocardial blood flow when used prior to exercise, increased myocardial oxygen demand, dose-related hypokalemia, unmasking of channelopathies, and suppressing sodium channel conduction. (Goldfarb M et al. Review of published cases of adverse cardiovascular events after ingestion of energy drinks. 2014 Am J Cardiol 113:168-172)

**Monday, April 28, 2014**

**Question:**

Baclofen is commonly used to treat muscular spasms in patients with spinal cord injuries and neurological disorders and has recently been reported to have use in preventing relapse in cocaine dependent male individuals. What is the proposed mechanism for these effects?

**Answer:**

So-called drug cues, even subliminal ones, can trigger people with drug addiction to seek and participate in drug use. Baclofen is posited to interfere with the brain's early response to subliminal drug cues and may stunt the internal processing of drug related cues that can lead to drug relapse. (Young KA et al. Nipping cue reactivity in the bud: baclofen prevents limbic activation elicited by subliminal drug cues. 2014 J Neuroscience 34(14): 5038-5043)

**Friday, April 25, 2014**

**Question:**

In what industries does one find the chemical paranitroaniline, what is the primary toxicity of this chemical and what are the most important routes of exposure for this chemical?

**Answer:**

Paranitroaniline is frequently used as an intermediate in the manufacture of dyes. The cited reference also points out that it is used "in the production of rubber, gasoline, pesticides, paints and varnishes." Paranitroaniline is acutely toxic to the hematopoietic system as a strong methemoglobin former. The authors of the cited reference also point out that paranitroaniline is fat soluble and readily absorbed through intact skin. "Exposures most commonly occur via the skin and lungs although ingestion has also been reported." (Fagan K et al. Paranitroaniline poisoning: A failure in basic prevention? 2014 JOEM 56(1): 112-114)

**Thursday, April 24, 2014**

**Question:**

Why is hypercarbia a relatively late finding in cases of infant botulism?

**Answer:**

The authors of the cited reference note: "The neuromuscular junction has a large margin of safety, and the clinical features of infant botulism are often not apparent until a substantial proportion of receptors are affected by botulinum toxin. Before weakness is detected clinically, roughly 75% of receptors need to be occupied by a neuromuscular blocking agent, and diaphragmatic function may not be affected until 90% to 95% of receptors are occupied; therefore, hypercarbia is usually a relatively late clinical finding in infant botulism." (Domino RM et al. Infant botulism: Two recent cases and literature review. 2008 J Child Neurol 23(11): 1336-1346)

**Wednesday, April 23, 2014**

**Question:**

Accidental envenomation by the stonefish (genus *Synanceia*) is not an uncommon occurrence in a variety of coastal waters around the world (including cold coastal waters of the US). How does the stonefish deliver venom, what are the clinical effects of the venom delivered by this animal and what treatment is recommended for stonefish envenomation?

**Answer:**

The stonefish has 13 very sharp, erectile, dorsal spines, 3 anal spines and 2 pelvic spines capable of penetrating skin. The stonefish venom is released from paired venom glands at the base of these spines and delivered via the spines. The cited reference notes that the toxin itself "may cause myotoxic, cardiotoxic, and neurotoxic effects as well as hemolysis and vascular leakage." This envenomation also causes excruciating pain and local edema. According to the reference, "Recommendations for acute treatment include analgesia and fluid resuscitation, removal of any residual spines and immersion of the body part in 45 degree (Centigrade) water in an attempt to denature the venom protein." The authors note that anti-venom "does exist but the indications for its use are controversial. Although it can rapidly relieve symptoms, it can be associated with life threatening side-effect such as anaphylaxis or delayed serum sickness." Surgical debridement and antibiotic therapy may be required for cases involving severe envenomations with tissue necrosis. Death is possible following severe envenomations. Interestingly, many stonefish envenomations are occupational injuries occurring in the fishing industry. (Dall GF et al. Severe sequelae after stonefish envenomation. 2006 The Surgeon 4(6): 384-385)

**Tuesday, April 22, 2014**

**Question:**

Sea urchin envenomation is not an uncommon problem for swimmers, divers, and people walking on beaches in tropical and subtropical areas. What are the usual clinical manifestations of sea urchin envenomation when skin contact with these sea creatures occurs?

**Answer:**

Following skin penetration by sea urchin spines, varying degrees of pain develop within minutes and may last as long as 24 hours. In some cases the pain may be severe. The skin surrounding any embedded spines may be erythematous and local edema may develop. The author of the cited reference notes: "In rare cases systemic effects such as nausea, weakness, palpitations, syncope, bronchospasm, muscle paralysis and respiratory distress may occur." The author of the cited reference further notes: "Cranial nerve dysfunction and hepatitis have been reported. Within days of injury a pruritic eruption may appear due to delayed hypersensitivity reaction, while months later chronic granuloma formation can occur." (Morocco A. Sea urchin envenomation. 2005 Clin Tox 43(2): 119-120)

**Monday, April 21, 2014**

**Question:**

What percentage of all foodborne disease in the US is attributable to the ingestion of seafood? Which seafood is responsible for the majority of seafood-related foodborne illness in the US? Which bacterium is responsible for the majority of seafood related deaths?

**Answer:**

The cited reference notes that while seafood comprises less than one percent of the typical Americans' diet, seafood is responsible for roughly 25% of all foodborne disease in the US. The authors go on to point out "despite the variety of seafoods we eat, 96% of all seafood diseases are due to ingestion of raw oysters, and 95% of all seafood related deaths are due to a single bacterium, *Vibrio vulnificus*." (Oliver JD. *Vibrio vulnificus*: Death in the half shell. A personal journey with the pathogen and its ecology" 2013 Microb Ecol 65:793-799)

**Friday, April 18, 2014**

**Question:**

What are the most common potential sources for the toxin aconitine?

**Answer:**

While aconitine has been reported be found in some traditional Chinese and Japanese herbal medicines, aconitine is primarily found in the plant known as Monkshood (*Aconitum napellus*). (Pullella R et al. A case of fatal aconitine poisoning by Monkshood ingestion. 2008 J Forensic Sci 53(2): 491-494)

**Thursday, April 17, 2014****Question:**

What are so called "thickened" nerve agents?

**Answer:**

The cited reference notes that "At normal temperatures, the nerve agents are liquids. Melting points range from minus 42°C (soman) to minus 39°C (VX)." They go on to point out "Thickening agents, such as acrylates, can be added to some nerve agents. This alters some of the physical properties of the resultant mixture, thus increasing its persistency in the environment." (Leikin JB et. al. A review of nerve agent exposure for the critical care physician. 2002 Crit Care Med 30(10): 2346-2354)

**Wednesday, April 16, 2014****Question:**

Atrazine is an "RUP" What is atrazine and what is an "RUP"?

**Answer:**

Atrazine is the common name for an herbicide that is widely used to kill weeds. It is used mostly on farms. Pure atrazine-an odorless, white powder-is not very volatile, reactive, or flammable. It will dissolve in water. Atrazine is made in the laboratory and does not occur naturally. Atrazine is used on crops such as sugarcane, corn, pineapples, sorghum, and macadamia nuts, and on evergreen tree farms and for evergreen forest regrowth. It has also been used to keep weeds from growing on both highway and railroad rights-of-way. Atrazine can be sprayed on croplands before crops start growing and after they have emerged from the soil. Some of the trade names of atrazine are Aatrex®, Aatram®, Atratol®, and Gesaprim®. The scientific name for atrazine is 6-chloro-N-ethyl-N'-(1-methylethyl)-triazine-2,4-diamine. Atrazine is a Restricted Use Pesticide (RUP), which means that only certified herbicide users may purchase or use atrazine. Certification for the use of atrazine is obtained through the appropriate state office where the herbicide user is licensed. (<http://www.atsdr.cdc.gov/phs/phs.asp?id=336&tid=59>)

**Tuesday, April 15, 2014****Question:**

The development of cerebral calcifications is an uncommon complication of the intrathecal (and perhaps oral) administration of what drug?

**Answer:**

Cerebral calcifications have been associated with intrathecal methotrexate therapy. (Mueller S et al. Cerebral calcifications associated with intrathecal methotrexate therapy in acute lymphocytic leukemia. 1976 J Pediatr 88(1): 650-653 and NEJM Image Challenge at <http://www.nejm.org/image-challenge>)

**Monday, April 14, 2014****Question:**

Chloroacetophenone (CN), the active ingredient of Mace, is a riot control or tear agent used by the military and law enforcement. It is also available to the general public. What is the odor often attributed to this agent?

**Answer:**

Chloroacetophenone (CN) has a sharp, irritating odor, sometimes described as "apple blossoms" odor. ([http://www.cdc.gov/niosh/ershdb/EmergencyResponseCard\\_29750033.html](http://www.cdc.gov/niosh/ershdb/EmergencyResponseCard_29750033.html))

**Friday, April 11, 2014****Question:**

Sodium azide (NaN<sub>3</sub>) [crystals or powder] is a chemical with no color, odor or taste. It is easily soluble in water and when added to water forms hydrazoic acid (HN<sub>3</sub>). Human exposure to sodium azide has often been associated with suicide ingestions or occupational exposures. What are the clinical characteristics due to poisoning with sodium azide?

**Answer:**

The authors of the cited reference note that the toxicity associated with sodium azide poisoning are dose dependent. They further note that "Lower doses cause hypotension, palpitations, tachycardia, dyspnea, headaches, syncope, diaphoresis, nausea and vomiting whereas higher doses cause prolonged or recurrent hypotension, seizures, dysrhythmias, acidosis and death." (Schwarz ES et al. Multiple poisonings with sodium azide at a local restaurant 2013 J Emerg Med 46(4): 491-494)

**Thursday, April 10, 2014****Question:**

Ricin is one of a number of toxins of plant and bacterial origin collectively referred to as ribosome inactivating proteins (RIPs). They are so named for their ability to depurinate the alpha-sarcin/ricin loop (SRL) of the large rRNA and inhibit protein synthesis. What are the other members of this group of toxins?

**Answer:**

The cited reference notes that the following substances are also members of the ribosome inactivating protein toxins: "the plant toxin pokeweed antiviral protein (PAP) (from *Phytolacca americana*), trichosanthin (TCS) (from *Trichosanthes kirilowii*), abrin (from *Abrus precatorius*), saporin (from *Saponaria officinalis*), gelonin (from *Gelonium multi- florum*), and Shiga toxins (Stx) found in the bacterial species *Shigella dysenteriae* and Shiga-toxigenic *Escherichia coli*." (May KL et al. Targeting ricin to the ribosome. 2013 Toxinon 69:143-151)

**Wednesday, April 9, 2014****Question:**

Are there any venomous mammals? If so, what are they?

**Answer:**

The cited reference reports “The taxonomically complex group Insectivora holds most of the venomous mammals. With the exception of vampire bats, these are the only mammals so far observed to produce toxic saliva. The American short- tailed shrew (*Blarina brevicauda*), the Hispaniolan sol- enodon (*Solenodon paradoxus*), the European water shrew (*Neomys fodiens*) and the Mediterranean water shrew (*Neomys anomalus*) provided the most definite evidences for salivary venom. Preliminary studies suggest that the Cuban solenodon (*Solenodon cubanus*) and the Canarian shrew (*Crocidura canariensis*) also produce venomous saliva. Suspicion remains upon untested insectivores, including the American shrew (*Sorex cinereus*) and the European mole (*Talpa europaea*). Moles have large and granular submaxillary glands and are known for storing worms in “paralyzed” state in their burrows. Hedgehogs were once considered venomous, but subsequent tests revealed no toxicity in their saliva.” (Ligabue-Braun R et al. Venomous mammals: A review. 2012 Toxicon 59:680-695)

**Tuesday, April 8, 2014****Question:**

Grayanotoxins, also known as andromedotoxin, acetylandromedol or rhodotoxin, are derived from the leaves, twigs or flowers of plants belonging to genera of the Ericaceae (heath) family, comprising among others the *Rhododendron*, *Pieris*, *Agarista* and *Kalmia* genera. What is the primary toxicity of grayanotoxin?

**Answer:**

The cited article notes: “The toxicity of grayanotoxin lies in its ability to bind to the group II receptor site in voltage gated sodium channels within the cell.” The authors further point out that “grayanotoxin binding modifies the channels configuration to such an extent that it prevents sodium channel inactivation, rendering the cell in a depolarized, and thus, activated state. Grayanotoxins bind to the channel only in its open state and, thereafter, the activation potential of the modified sodium channel is shifted in the direction of hyperpolarization.” (Jansen SA et al. Grayanotoxin poisoning: ‘Mad honey disease’ and beyond. 2012 Cardiovasc Toxicol 12:208-215)

**Monday, April 7, 2014****Question:**

What clinical circumstances were associated with the first descriptions of aluminum toxicity in adults? In pediatric patients?

**Answer:**

The cited references report “Aluminum toxicity was first described in adults with end-stage renal disease who were undergoing dialysis using dialysate made from water with elevated aluminum content. These patients developed dialysis encephalopathy and osteomalacia which was related to the duration of dialysis therapy. In addition, patients had significant elevations in serum aluminum concentrations and those suffering from dialysis encephalopathy had elevated brain-aluminum concentrations. The first reports of pediatric patients having similar symptoms emerged from children with renal dysfunction who were being treated with aluminum-containing phosphate binders but were not receiving dialysis.” (Alfrey AC et al. The dialysis encephalopathy syndrome. 1976 NEJM 294:184-188 as cited in Wier HA and Kuhn RJ. Aluminum toxicity in neonatal parenteral nutrition: What can we do? 2012 Ann Pharmacother 46:137-140)

**Friday, April 4, 2014****Question:**

Dapsone is one of the most common causes for acquired methemoglobinemia. When dapsone is used for the treatment of dermatological conditions (e.g. pemphigus) some authorities recommend the use of concurrent administration of what drug to reduce the risk for the development of methemoglobinemia?

**Answer:**

Some authorities have recommended a concurrent course of cimetidine when dapsone is used for the treatment of various skin conditions. The cited reference reports “Cimetidine, by virtue of its inhibitory action on cytochrome P450 (chiefly 2C19) isoenzymes, decreased dapsone’s metabolism to its toxic hydroxylamine metabolite with an attendant 27% reduction in the baseline methemoglobinemia level. (Barclay JA et al. Dapsone-induced methemoglobinemia: A primer for clinicians. 2012 Ann Pharmacother 45:1103-1115)

**Thursday, April 3, 2014****Question:**

While most benzodiazepine overdose cases are managed by the use of airway control and supportive care, in selected cases, some clinicians may opt to use the reversal agent flumazenil. What is the recommended dose of flumazenil when used for the management of suspected benzodiazepine overdose in adults?

**Answer:**

According to the package insert for Flumazenil Injection, USP, “For initial management of a known or suspected benzodiazepine overdose, the recommended initial dose of flumazenil injection is 0.2 mg (2 mL) administered intravenously over 30 seconds. If the desired level of consciousness is not obtained after waiting 30 seconds, a further dose of 0.3 mg (3 mL) can be administered over another 30 seconds. Further doses of 0.5 mg (5 mL) can be administered over 30 seconds at 1-minute intervals up to a cumulative dose of 3 mg. Most patients with a benzodiazepine overdose will respond to a cumulative dose of 1 mg to 3 mg of flumazenil injection, and doses beyond 3 mg do not reliably produce additional effects. On rare occasions, patients with a partial response at 3 mg may require additional titration up to a total dose of 5 mg.” (<http://www.west-ward.com/images/files/package/Flumazenil%20PI.pdf>)

**Wednesday, April 2, 2014****Question:**

With acute opioid overdose and heroin related deaths at high levels nationwide, many first responders (including police) are now carrying naloxone for intranasal administration. What is the usual dose of intranasal naloxone?

**Answer:**

The cited reference reports “The usual intranasal dose [of naloxone] (off label) is 2 mg (1 mg per nostril) which can be repeated in 3-5 minutes.” (The Medical Letter, March 17, 2014, 56(1438): 21-22)

**Tuesday, April 1, 2014****Question:**

What is the pathophysiologic basis of cocaine-related renal injury?

**Answer:**

According to the cited article, “The pathophysiologic basis of cocaine-related renal injury is multifactorial and involves changes in renal hemodynamics, changes in glomerular matrix synthesis, degradation and oxidative stress and induction of renal atherogenesis.” (Jaffe JA and Kimmel PL. Chronic nephropathies of cocaine and heroin abuse: A critical review. 2006 Clin J Am Soc Nephrol 1:655-667)



**Monday, March 31, 2014**

**Question:**

Acrylamide (ACR) is a water-soluble alkene used in the production of a variety of commercial polymers and gels. Polyacrylamide compounds are often used in the cosmetic, paper, and textile industries; in ore processing; and as soil conditioners and flocculants for wastewater treatment. During the 1950s it became apparent that occupational exposure to ACR had the potential to cause toxicity. Which organ system is involved and what characterizes the toxicity associated with ACR?

**Answer:**

High-level, long duration, occupational ACR exposure has the potential, in some cases, to cause a neurotoxic syndrome characterized by ataxia, skeletal muscle weakness, cognitive impairment and numbness of the extremities. (LoPachin RM and Gavin T. Molecular mechanism of acrylamide neurotoxicity: Lessons learned from organic chemistry. 2012 Env Health Perspect 120:1650-1657)

**Friday, March 28, 2014**

**Question:**

In 1956 the drug Bendectin was approved to treat the nausea and vomiting of pregnancy. Eventually allegations arose implicating this drug as a teratogen. What was the original formulation of Bendectin? What were the primary teratogenic allegations (that were eventually disproven)?

**Answer:**

The cited reference notes that Bendectin was a three-agent formulation, consisting of 10 mg of dicyclomine hydrochloride (an antispasmodic agent), 10 mg of doxylamine succinate (an antihistamine), and 10 mg of pyridoxine hydrochloride (vitamin B6). Limb-reduction deformities, cardiac defects, oral clefts, and genital tract malformations were among the conditions alleged to be associated with Bendectin use. (Slaughter SR et al. FDA approval of doxylamine-pyridoxine therapy for use in pregnancy. 2014 NEJM 370:1081-1083)

**Thursday, March 27, 2014**

**Question:**

Norbormide is a rodenticide with unique specificity of action. How does this agent kill rats?

**Answer:**

The toxicity of norbormide in the rat is due to tissue ischemia resulting from generalized vascular constriction. This effect occurs essentially exclusively in the relatively small caliber arteries (e.g. mesenteric and coronary) of the rat. Interestingly, the drug does not cause aortic constriction. (Bova S et al. Vasorelaxant properties of norbormide, a selective vasoconstrictor agent for the rat microvasculature. 1996 Br J Pharm 117:1041-1046)

**Wednesday, March 26, 2014**

**Question:**

Approximately 11.3 million persons (or 3.7% of the 308.7 million U.S. population) live within 150 meters of a major highway. Numerous epidemiologic studies have consistently demonstrated that living close to major roads or in areas of high traffic density is associated with adverse health effects. What are these adverse health effects?

**Answer:**

The adverse health effects associated with living in proximity to major roadways include asthma, chronic obstructive pulmonary disease, and other respiratory symptoms, cardiovascular disease risk and outcomes, adverse reproductive outcomes and mortality. (Boehmer TK et al. Residential proximity to major highways — United States, 2010 MMWR November 22, 2013 / 62(03); 46-50)

**Tuesday, March 25, 2014**

**Question:**

What is NMAM?

**Answer:**

NMAM is a collection of methods for sampling and analysis of contaminants in workplace air, and in the blood and urine of workers who are occupationally exposed. These methods have been developed or adapted by NIOSH or its partners and have been evaluated according to established experimental protocols and performance criteria. NMAM also includes chapters on quality assurance, sampling, portable instrumentation, etc. (<http://www.cdc.gov/niosh/docs/2003-154/>)

**Monday, March 24, 2014**

**Question:**

Stainless steel is primarily composed of iron but also contains small quantities of chromium (18%), nickel (9-11%), manganese (1-2%) and cobalt (trace). Is it possible to see elevated levels of these elements as a result of blood specimens being drawn through stainless steel needles?

**Answer:**

The authors of the cited study looked at trace element contamination of blood samples by stainless steel venipuncture needles compared with plastic cannulas. They reported no significant difference between the metal concentrations measured from blood draws using different (standard stainless steel needles versus plastic cannula. These investigators concluded "It is not necessary to routinely use a plastic cannula for blood sampling for trace element analysis. However, it is possible that sporadic contamination due to stainless steel needles may occur, so we recommend that unexpected high concentrations are verified by taking a second sample taken through a plastic cannula." (Hodnett D et al. A healthy volunteer study to investigate trace element contamination of blood samples by stainless steel venipuncture needles. 2012 Clin Tox 50(2): 99-107)

**Friday, March 21, 2014**

**Question:**

What is toxaphene?

**Answer:**

Toxaphene was one of the most heavily used pesticides in the United States in the 1970s and early 1980s. It was used primarily to control insect pests on cotton and other crops in the southern United States. Other uses included controlling insect pests on livestock and killing unwanted fish in lakes. Toxaphene was banned for all registered uses by 1990. Toxaphene is made by reacting chlorine gas with a substance called camphene. The resulting product (toxaphene) is a mixture of hundreds of different chlorinated camphenes and related chemicals. (<http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=99>)

**Thursday, March 20, 2014****Question:**

Coughing often occurs after the administration of intravenous fentanyl to patients during anesthesia induction. What are the possible mechanisms for fentanyl-related cough?

**Answer:**

According to the cited reference, “The rapid cough response elicited by bolus fentanyl suggests that the pulmonary chemo-reflex resulting from stimulation of C-fiber receptors (J receptors) may play a role in fentanyl-induced cough.” Fentanyl triggers smooth muscle constriction in the trachea, thus stimulation of irritant receptors (rapidly adapting receptors) secondary to deformation of the tracheobronchial wall may also be at play. The authors also point out “Selective beta-adrenergic bronchodilators (terbutaline and salbutamol) or NMDA antagonists (ketamine) have been reported to reduce the incidence of fentanyl-induced cough, providing support for the possible role of bronchoconstriction.” Another possible mechanism may involve histamine release from pulmonary mast cells as inhalation of sodium cromoglicate has been shown to decrease the incidence of cough. In addition, sudden adduction of the vocal cords or supraglottic obstruction by soft tissue due to opioid-induced muscle rigidity may also play a role. (Hung KC et al. The effect of pre-emptive use of minimal dose fentanyl on fentanyl-induced coughing. 2010 Anesthesia 65:4-7)

**Wednesday, March 19, 2014****Question:**

What is lepidopterism?

**Answer:**

Some caterpillar members of the species Lepidoptera have larvae with poisonous hairs or “setae”. These setae contain an urticating toxin that can cause skin and mucous membrane reactions on contact. The cited reference notes “Cutaneous reactions of lepidopterism are of three different types: weal and flare reaction, toxic irritant dermatitis, and persistent itchy papules. Other signs are conjunctivitis, pharyngitis, malaise, and upper respiratory tract symptoms including respiratory distress.” Some cases involving life threatening anaphylactic reactions have been reported. (Gottschling S and Meyer S. An epidemic airborne disease caused by the oak processionary caterpillar. 2006 Pediatric Derm 23(1): 64-66)

**Tuesday, March 18, 2014****Question:**

An increased risk for adverse cardiovascular events has been reported with some NSAIDs. Which currently available NSAID is thought to be associated with the highest risk of serious cardiovascular events?

**Answer:**

Diclofenac is the NSAID thought to be associated with the highest risk of serious cardiovascular events. (The Medical Letter, 2014, 56(1437):19-20)

**Monday, March 17, 2014****Question:**

What is Samter’s triad?

**Answer:**

Samter’s triad is a clinical syndrome characterized by aspirin sensitivity, nasal polyps, and bronchial asthma. The cited reference points out that this is also known as “aspirin exacerbated respiratory disease” or “aspirin sensitive asthma”. The authors note that in this syndrome exposure to aspirin or other cyclooxygenase-I inhibitors results in a spectrum of bronchospasm, laryngospasm, rhinitis, and conjunctivitis. The mechanism for this aspirin intolerance has not been fully elucidated but likely relates to accumulation of leukotrienes and other inflammatory products resulting from dysfunction of the arachidonic acid metabolism pathway. (Shen J et al. Aural polyps in Samter’s triad: Case report and literature review. 2012 Otolaryngology and Neurology 33:774-778)

**Friday, March 14, 2014****Question:**

What is the incidence of peptic ulcer disease and bleeding complications related to therapeutic doses of aspirin?

**Answer:**

The cited reference notes that “even with therapeutic doses of acetylated salicylic acid there is a peptic ulcer incidence of 5-10% over 3-6 months of usage and a bleeding complication rate of 0.5-2.0 per 100 patient years. (Duthie GG and Wood AD. Natural salicylate: foods, functions and disease prevention. 2011 Food Funct 2:515-520)

**Thursday, March 13, 2014****Question:**

The rate of suicide among physicians is higher than that of the public at large. How prevalent is self-poisoning as a means for committing suicide among physicians?

**Answer:**

According to the cited reference: “For physicians, firearms were the most common method (48%), followed by poisoning (23.5%), blunt trauma (14.5%), and asphyxia which included hanging (14%).” (Gold KJ et al. (2013) Details on suicide among US physicians: data from the National Violent Death Reporting System 35:45-49)

**Tuesday, March 11, 2014****Question:**

What is the primary use for zincdiethyldithiocarbamate (ZDEC) in laboratory toxicological research?

**Answer:**

Zincdiethyldithiocarbamate (ZDEC) is commonly used as a standard for in vitro cytotoxicity testing. (Rosengren A et al. Comparison of implantation and cytotoxicity testing for initially toxic biomaterials. 2005 J Biomed Mat Res Part A. 75(1):115-122)

**Monday, March 10, 2014****Question:**

What is the relationship between silica exposure and the development of tuberculosis?

**Answer:**

According to the cited reference, "Tuberculosis risk increases with severity of silicosis and in acute and accelerated silicosis." These authors go on to state: "Silica exposure increases tuberculosis risk even without silicosis." (Leung CC et al. Silicosis. 2012 Lancet 379:2008-2018)

**Friday, March 7, 2014****Question:**

What is the association between marijuana smoking and stroke?

**Answer:**

The authors of the cited reference state "Cases of clear, documented stroke during marijuana use have been previously reported. Later reports confirmed this association, finding that strokes tend to occur during actual marijuana inhalation in episodic and heavy marijuana users." These authors go on to state that "mechanisms underlying adverse cerebrovascular events may also include cerebral vasoconstriction". They observe that on transcranial Doppler sonography, marijuana appears to increase vascular resistance and velocity in users when compared with non users. (Thomas G et al. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana inhalation: What cardiologists need to know. 2014 Am J Cardiol 113:187-190)

**Thursday, March 6, 2014****Question:**

What are phthalates?

**Answer:**

Phthalates are a group of aromatic chemicals containing a phenyl ring with two attached and extended acetate groups. They are typically colorless liquids used to make plastics more flexible and resilient, and are often referred to as plasticizers. Because they are not a part of the chain of chemicals (polymers) that makes up plastics, they can be released fairly easily from these products. These plastics are found in products such as toothbrushes, automobile parts, tools, toys, and food packaging. Some are also used in cosmetics, insecticides, and aspirin. Examples include Di(2-ethylhexyl)phthalate (DEHP), Di-n-butyl Phthalate, Di-n-octylphthalate (DNOP) and Diethyl phthalate. (<http://www.atsdr.cdc.gov/substances/toxchemicallisting.asp?sysid=41>; accessed February, 2014)

**Wednesday, March 5, 2014****Question:**

What is lathyrism and what chemical has been widely assumed to be causative of this disorder?

**Answer:**

Lathyrism is a disorder associated with the ingestion of the grass pea (*Lathyrus sativus*). According to the cited reference, the main clinical sign is "a permanent, but not progressive, bilateral symmetric paraparesis which emerges in association with consumption of grass pea products as the main (or sole) food item for several weeks, due to the lack of availability of alternative foods."

The authors go on to point out that "The association of lathyrism with grass pea (consumption) is firmly established, but the causative agents and pathogenic mechanisms remain doubtful. *L. sativus* seeds contain large amounts of b-N-oxalyl-L-a,b-diaminopropionic acid (ODAP), and this non-protein amino acid is widely accepted as the likely causative agent of lathyrism." (Llorens J et al A new unifying hypothesis for lathyrism, konzo and tropical ataxic neuropathy: Nitriles are the causative agents. 2011 Food and Chemical Toxicology 49:563-570)

**Tuesday, March 4, 2014****Question:**

What is the U.S. Chemical Safety Board?

**Answer:**

The Chemical Safety Board (CSB) is an independent federal agency charged with investigating industrial chemical accidents. Headquartered in Washington, DC, the agency's board members are appointed by the President and confirmed by the Senate. The CSB conducts root cause investigations of chemical accidents at fixed industrial facilities. Root causes are usually deficiencies in safety management systems, but can be any factor that would have prevented the accident if that factor had not occurred. Other accident causes often involve equipment failures, human errors, unforeseen chemical reactions or other hazards. The agency does not issue fines or citations, but does make recommendations to plants, regulatory agencies such as the Occupational Safety and Health Administration (OSHA) and the Environmental Protection Agency (EPA), industry organizations, and labor groups. Congress designed the CSB to be non-regulatory and independent of other agencies so that its investigations might, where appropriate, review the effectiveness of regulations and regulatory enforcement. (<http://www.csb.gov/about-the-csb/>; accessed February, 2014)

**Monday, March 3, 2014****Question:**

Manure pit systems are used primarily on livestock farms (including dairy operations) to allow for the easy cleaning of animal confinement buildings and the efficient underground storage of large amounts of raw manure. Inside the pit, the manure undergoes anaerobic digestive fermentation to form fertilizer. The digestive process can generate four potentially dangerous gases; what are they?

**Answer:**

The four potentially hazardous gases usually associated with manure pits are: methane, hydrogen sulfide, carbon dioxide and ammonia. The National Traumatic Occupational Fatality (NTOF) Data Base indicates that from 1980 through 1985, 16 deaths resulted from the asphyxiation (suffocation) of workers in manure pits or similar waste tanks. (<http://www.cdc.gov/niosh/docs/90-103/>; accessed February 2014))

**Friday, February 28, 2014**

**Question:**

Which commonly used chemotherapeutic agents are associated with the development of chemotherapy-induced peripheral neuropathy (CIPN), a serious and dose limiting side effect? What are the characteristics of CIPN?

**Answer:**

The authors of the cited article report that CIPN is often associated with platinum agents, taxanes, vinca alkaloids, thalidomide, bortezomib and ixabepilone. They further state “CIPN commonly occurs in 30-40% of patients but its incidence can vary from 0 to 70%. The symptoms most commonly associated with CIPN are sensory neuropathies including parenthesis and pain. Symptoms often start in the fingers and toes and spread proximally in a “glove and stocking” distribution. CIPN can begin weeks to months after initial treatment and reach a peak at, or after, the end of treatment.” In some cases the symptoms resolve once treatment ceases but in most cases CIPN is not completely reversible and can indeed be permanent. (Pachman DR et al. Chemotherapy induced peripheral neuropathy: Prevention and treatment. 2011 Clin Pharm Ther 90(3):377-387)

**Thursday, February 27, 2014**

**Question:**

What are the usual causes of death from acute colchicine poisoning?

**Answer:**

The cited reference notes “Death from acute colchicine poisoning is usually due to hemodynamic collapse and cardiac arrhythmias (typically 24–36 h after ingestion or could be sudden) or from infectious or hemorrhagic complications. (Finkelstein Y et al. Colchicine poisoning: the dark side of an ancient drug. 2010 Clin Tox 48(5):407-414)

**Wednesday, February 26, 2014**

**Question:**

Exposure to what toxicant is posited by some to be the cause of the deafness suffered by Ludwig Van Beethoven?

**Answer:**

The cited reference points out “Recent analysis of his (Beethoven’s) hair and bone has determined that he had lead poisoning”. They further point out that “A lock of his hair removed at the time of his death, and stored in an airtight case, was analyzed in 2000 by researchers in Illinois. Beethoven’s parietal skull bone was later analyzed in 2005. Both showed markedly elevated lead levels consistent with lead poisoning. As for the potential source for lead exposure in the case of Beethoven, the authors posit “It is well known that at that time lead was added illegally to inexpensive wine to improve the flavor. Beethoven was particularly fond of the adulterated or fortified Hungarian wine. It has been suggested that after the death of Beethoven’s mother when he was 17 years old, he began to use wine to help deal with his loss.” These authors have concluded that Beethoven’s chronic consumption of wine tainted with lead is the best explanation for his hearing loss. (Stevens MH et al. Lead and the deafness of Ludwig Van Beethoven. 2013 The Laryngoscope 123:2854-2858)

**Tuesday, February 25, 2014**

**Question:**

What is ochratoxin A?

**Answer:**

Ochratoxin A (OTA) is a mycotoxin formed primarily by some species of *Aspergillus* and *Penicillium*. OTA has been shown to be carcinogenic, nephrotoxic, teratogenic, immunotoxic, and hepatotoxic in various experimental animal models, and the International Agency for Research on Cancer (IARC) classifies it as possibly carcinogenic to humans (group 2B). OTA is found in grains and a variety of other food-stuffs including cocoa and cocoa products. (Turcotte A et al. Analysis of cocoa products for ochratoxin A and aflatoxins. 2013 Mycotoxin Res 29:193-201)

**Monday, February 24, 2014**

**Question:**

What is the effect of cinnamon ingestion on postprandial blood glucose levels?

**Answer:**

The authors of the cited reference concluded, “Findings from the current study provide support for the hypoglycemic effect of cinnamon in healthy individuals during the postprandial period. Critical questions for future research are (a) whether the reduction of blood glucose is maintained with long-term cinnamon supplementation and (b), if so, whether the reduction can delay or prevent the development of type 2 diabetes mellitus and related disease states.” (Magistrelli A and Chezem JC. Effect of ground cinnamon on postprandial blood glucose concentration in normal-weight and obese adults. 2012 J Acad Nutrition and Dietetics. 112(11):1806-1809)

**Friday, February 21, 2014**

**Question:**

What is Haff disease and what toxin is associated with this disorder?

**Answer:**

Haff disease involves the development of rhabdomyolysis and muscle weakness after consumption of fresh water fish. According to the cited reference, cases have “rarely been reported in the United States but have been frequently reported from the Baltic region”. The authors point out “While the etiology is unknown, it is felt to be a toxin. Palytoxin, found in marine fish, has been associated with rhabdomyolysis, and may serve as a model for further study of the suspected toxin responsible for rhabdomyolysis after consumption of fresh water fish.” (Langley RL and Bobbitt WH. Haff disease after eating salmon. 2007 Southern Med Journal 100(11): 1147-1150)

**Thursday, February 20, 2014**

**Question:**

Drinking large amounts of coconut water has been associated with the development of which electrolyte abnormality?

**Answer:**

Coconut water contains a large concentration of potassium and thus ingestion of large amounts of coconut water may produce hyperkalemia in some individuals. (Rees RN et al. Coconut water-induced hyperkalemia. 2012 Br J Hosp Med 73(9): 534)

**Wednesday, February 19, 2014**

**Question:**

What is the effect of green tea and green tea catechins on cancer risk and what is the effect of green tea and green tea catechins on cardiovascular risk factors?

**Answer:**

A recent systematic review on these topics concluded: "The evidence for green tea and cancer risk is inadequate and inconclusive. However there is some positive evidence for risk reduction of breast, prostate, ovarian and endometrial cancers with green tea. Randomized control trials (RTC's) of green tea and cardiovascular risk factors suggest that green tea may reduce low-density lipoproteins and total cholesterol, although studies are of short duration. There is no robust evidence to support a reduction in coronary artery disease risk in green tea drinkers. There are a considerable number of RCTs to suggest that green tea does reduce body weight in the short term, but this not likely to be of clinical relevance." (Johnson R et al. Green tea and green tea catechin extracts: An overview of the clinical evidence. 2012 Maturitas 73:280-287)

**Tuesday, February 18, 2014**

**Question:**

Which occupational exposures have been proven to cause Parkinson's disease? What widespread inhalational exposure likely confers a reduced risk for the development of Parkinson's disease?

**Answer:**

In fact, no specific occupational exposures have been proven to cause Parkinson's disease. A recently published study looked at more than 14,000 workers in a 43-year prospective cohort study (in men). These investigators reported finding no association between Parkinson's disease or Parkinsonian disorders and occupational exposure to pesticides, welding smoke, metal dust, wood dust, animal handling, stone and concrete dust, chrome and nickel dust, quartz dust, organic dust, oil, asbestos, organic solvents and irritating gas. The authors did, however, recommend that inorganic dust should be explored further as a potential risk factor for Parkinson's disease. Smokers have been shown to have a reduced risk for the development of Parkinson's disease. (Fledman A et al. Occupational exposure in Parkinsonian disorders: A 43-year prospective cohort study in men. 2011 Parkinsonism and Rel Dis 17:677-682)

**Monday, February 17, 2014**

**Question:**

Epoxy resins are one of the most frequent causes of occupational allergic contact dermatitis. What component of these resins causes the majority of cases of allergic contact dermatitis?

**Answer:**

The majority of cases of ACD are caused by base resins, specifically diglycidyl ethers of bisphenol A (DGEBA). (Cahill J et al. Prognosis of contact dermatitis in epoxy resin workers. 2005 Contact Dermatitis 52:147-153)

**Friday, February 14, 2014**

**Question:**

What is the generally accepted prevalence of occupational asthma?

**Answer:**

The cited reference reports "Occupational asthma has been reported in a minority of workers exposed to most known sensitizing agents (usually 10% or less among current workers in cross-sectional studies)". (Tarlo SM and Lemiere C. Occupational asthma 2014 NEJM 370:640-649)

**Thursday, February 13, 2014**

**Question:**

Sofosbuvir (Sofaldi) is a nucleotide polymerase inhibitor recently approved in the US for use in the treatment of chronic hepatitis C. What effect does this drug have with regard to the CYP450 enzymes?

**Answer:**

The cited reference notes: "Unlike protease inhibitors, sofosbuvir and its metabolites are not inhibitors, inducers or substrates of the CYP450 enzymes." (The Medical Letter, January 20, 2014, 56(1434): 5-6)

**Wednesday, February 12, 2014**

**Question:**

What are so-called MRLs and what organization promulgates MRLs?

**Answer:**

MRLs are "minimal risk levels" and they are developed and promulgated by the ATSDR. The ATSDR Minimal Risk Levels (MRLs) were developed as an initial response to The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse non-cancer health effects over a specified duration of exposure. (<http://www.atsdr.cdc.gov/mrls/index.asp>; accessed January 2014)

**Tuesday, February 11, 2014**

**Question:**

In the 1920's ENT pioneer Chevalier Jackson, MD, undertook a public campaign to be sure that proper warning labeling of containers containing what chemical was mandated by law?

**Answer:**

The cited reference points out that during the 1920's Dr. Chevalier Jackson began a public campaign to assure proper warning labels for commercial products containing caustics and as a result, the Federal Caustic Act of 1927 was enacted. (Riffat F and Cheng A. Pediatric caustic ingestion: 50 consecutive cases and a review of the literature. 2009 Diseases of the Esophagus 22, 89-94)

**Monday, February 10, 2014**

**Question:**

There have been only a very limited number of cases of cobalt toxicity reported to be due to hip arthroplasty. What clinical situation has been reported to be the most common associated with cobalt toxicity in this setting?

**Answer:**

According to the cited reference, "There have been 13 documented cases of cobalt toxicity from hip arthroplasties in the literature: 7 were due to wear of metal-on-metal hip arthroplasties, while the others followed the revision of a fractured ceramic hip." (Tower S. Arthroprosthetic cobaltism: neurological and cardiac manifestations in two patients with metal-on-metal arthroplasty. 2010 J Bone Joint Surg Am 92:2847-51 as cited in Gilbert CJ et al. Hip pain and heart failure: The missing link. 2013 Canadian J Cardiology 29:638-639)

**Friday, February 7, 2014**

**Question:**

What is the effect of NSAIDs on the platelet inhibition effect of aspirin?

**Answer:**

According to the cited reference, "COX-1 affinity determines the interaction between NSAIDs and ASA on thrombocyte adhesion and aggregation. Ibuprofen and naproxen, but not etoricoxib or meloxicam, taken 2 h before ASA, significantly inhibit ASA's antithrombocyte effect." (Meek IL, et al Interference of NSAIDs with the thrombocyte inhibitory effect of aspirin: A placebo-controlled, ex vivo, serial placebo-controlled serial crossover study. 2013 Eur J Clin Pharmacol 69:365-371)

**Thursday, February 6, 2014**

**Question:**

Which potentially poisonous fish is also known as fugu, bok, or sea squab? What are the potentially lethal toxins that may be contained in this fish? What are the so-called safe sources of this fish as per recent Food and Drug Administration (FDA) communications?

**Answer:**

The potentially poisonous fish is also known as fugu, bok, or sea squab is puffer fish. The potentially lethal toxins that may be contained in this fish are tetrodotoxin and saxitoxin. The FDA is advising consumers only to eat puffer fish from two (2) known specific safe sources. These safe sources are 1) imported puffer fish that have been processed and prepared by specially trained and certified fish cutters in the city of Shimonoseki, Japan, and 2) puffer fish caught in the mid-Atlantic coastal waters of the United States, typically between Virginia and New York. Puffer fish from all other sources potentially contain deadly toxins and therefore are not considered safe.  
(<http://www.fda.gov/Food/RecallsOutbreaksEmergencies/SafetyAlertsAdvisories/ucm085529.htm>. Accessed January 2014)

**Wednesday, February 5, 2014**

**Question:**

What is "NIDA"?

**Answer:**

"NIDA" stands for National Institute on Drug Abuse. NIDA's mission is "to lead the Nation in bringing the power of science to bear on drug abuse and addiction. This charge has two critical components. The first is the strategic support and conduct of research across a broad range of disciplines. The second is ensuring the rapid and effective dissemination and use of the results of that research to significantly improve prevention and treatment and to inform policy as it relates to drug abuse and addiction." (<http://www.drugabuse.gov/about-nida>, accessed January 2014)

**Tuesday, February 4, 2014**

**Question:**

What is the drug known as "N bomb"?

**Answer:**

"N- bomb" (also known as 25I-NBOMe, 25C-NBOMe and 25B-NBOMe) is one street name for a variety of synthetic substances recently encounters on the designer drug market. These substances are sold online and through illicit channels and are commonly purported to be illicit hallucinogens such as LSD. 25I-NBOMe, 25C-NBOMe and 25B-NBOMe target the same 5-HT2A (serotonin) receptor as many other hallucinogens, including Schedule I hallucinogens like LSD, 2C-I, 2C-C and 2C-B. These substances have been encountered as powders, liquid solutions, laced on edible items and soaked onto blotter papers. (Drug Enforcement Administration Office of Diversion Control. Available at [http://www.deadiversion.usdoj.gov/drug\\_chem\\_info/nbome.pdf](http://www.deadiversion.usdoj.gov/drug_chem_info/nbome.pdf); accessed January 2014)

**Monday, February 3, 2014**

**Question:**

Bites from which snakes are reported to result in the development of multiple arterial thrombosis in up to 40% of envenomed patients?

**Answer:**

The "Fer de Lance" pit viper (*Bothrops lanceolatus*) and the related *Bothrops caribbaeus* are the only snakes whose bites are reported to cause multiple arterial thrombosis in up to 40% of envenomed persons. (Warrell DA, 2004. Snakebites in Central and South America: epidemiology, clinical features, and clinical management. *Bothrops lanceolatus*. Campbell JA, Lamar WW, eds. The Venomous Reptiles of the Western Hemisphere. New York: Cornell University Press; 743-744 as cited in Malbranque S et al. Case Report: Fatal Diffuse Thrombotic Microangiopathy after a Bite by the "Fer-de-Lance" Pit Viper (*Bothrops lanceolatus*) of Martinique. 2008 Am J Trop Hyg 78(6):856-861)

**Friday, January 31, 2014**

**Question:**

What is Feer Syndrome?

**Answer:**

Feer syndrome is also known as acrodynia or pink disease. The cited reference notes these syndromes are all related to elemental mercury and, less commonly, inorganic mercury salt intoxication primarily in children. (Mercer JJ, et al. Acrodynia and hypertension in a young girl secondary to elemental mercury toxicity acquired in the home. 2012 Pediatric Dermatology Vol. 29 No. 2 199-201)

**Thursday, January 30, 2014**

**Question:**

What are the potential adverse ocular effects related to inhalation of high concentrations of the chemical ethylene oxide?

**Answer:**

Based on studies in laboratory animals as well as scattered case reports there may be a concern for the development of ocular cataracts in individuals exposed to high concentrations of ethylene oxide for long periods. (<http://www.atsdr.cdc.gov/ToxProfiles/tp137-c2.pdf>; accessed January, 2014)

**Wednesday, January 29, 2014**

**Question:**

Recently a large number of cases of exposure to a substance named "black mamba" was reported in the state of Colorado. What is "black mamba"?

**Answer:**

"Black mamba" is a novel synthetic cannabinoid known as ADB-PINACA ((N-[1-amino-3,3-dimethyl-1-oxobutan-2-yl]-1-pentyl-1H-indazole-3-carboxamide). This substance has been reported to be associated with both neurotoxicity and cardiotoxicity. (Monte A, Bronstein A, Heard K and Iwanicki J. An outbreak of exposure to a novel synthetic cannabinoid. 2013 NEJM 37:389-390)

**Tuesday, January 28, 2014**

**Question:**

Some patients taking risperidone have been reported to develop gynecomastia and/or galactorrhea. What is the mechanism for this effect?

**Answer:**

The cited reference notes "Studies performed in adult patients unambiguously demonstrate a marked effect of risperidone on prolactin levels, with possible clinical effects related to hyperprolactinemia, such as gynecomastia and galactorrhea." (Holzer L and Eap CB. Risperidone-induced symptomatic hyperprolactinemia in adolescents. 2006 J Clin Psychopharmacol 26:167-171)

**Monday, January 27, 2014**

**Question:**

What is the reported risk for significant local or systemic effects following accidental digital injection of epinephrine?

**Answer:**

The authors of the cited paper report studying 365 epinephrine injections of the hand over a six-year period. Of these 213 were digital and 127 had follow up. They report all patients had "complete resolution of symptoms" and none required hospitalization. They further note "significant systemic effects were not reported". However, they do report "pharmacologic vasodilatory treatment was used in 23% of patients. Ischemic effects were documented for 4 patients. All 4 patients received vasodilator therapy and were discharged home with complete resolution of symptoms." (Muck AE et al. Six years of epinephrine digital injections: Absence of significant local or systemic effects. 2010 Anna Emerg Med 56(3): 270-274)

**Friday, January 24, 2014**

**Question:**

What is the biological basis for the seizure that can occur in association with isoniazid (INH)?

**Answer:**

The primary point to keep in mind is that GABA is an important inhibitory neurotransmitter in the central nervous system. The cited reference describes "Pyridoxal 5'-phosphate (the active form of vitamin B6) is a necessary coenzyme in the synthesis of GABA. Isoniazid depletes vitamin B6 by inhibiting pyridoxine phosphokinase, the enzyme that converts pyridoxine to its active form, pyridoxal 5'-phosphate. Isoniazid also reacts with pyridoxal 5'-phosphate to form an inactive complex that is renally excreted. This functional deficiency of pyridoxine in turn impairs the synthesis of GABA and increases susceptibility to seizures. The resulting seizures are often unresponsive to conventional anticonvulsant therapy (particularly phenytoin) and are best treated with intravenous pyridoxine to restore central nervous system GABA concentrations." (Minns AB et al. Isoniazid-induced status epilepticus in a pediatric patient after inadequate pyridoxine therapy. 2010 Pediatr Emerg Care 26:380-381)

**Thursday, January 23, 2014**

**Question:**

Aripiprazole (Abilify) is a quinolinone derivative atypical antipsychotic drug used primarily for adults with schizophrenia. At what receptors is this drug active?

**Answer:**

According to the cited reference, Aripiprazole has a unique receptor binding profile as it exhibits both partial agonist activity at dopamine D2 receptors and serotonin 5-HT1A receptors and antagonist activity at 5-HT2A receptors. (Croxtall JD. Aripiprazole: A review of its use in management of schizophrenia in adults. 2012 CNS Drugs 26(2): 155-183)

**Wednesday, January 22, 2014**

**Question:**

What are so-called "Brownfield sites"? What are land reuse sites?

**Answer:**

Brownfield sites are defined as "abandoned, idled, or underused industrial and commercial properties where reuse or redevelopment is complicated by real or perceived contamination." These sites have received funding from EPA Brownfield Program for redevelopment. Land Reuse sites are defined as "any site formally utilized for commercial and industrial purposes complicated by real or perceived contamination" that has not received funding from the EPA Brownfield Program for redevelopment. (<http://www.atsdr.cdc.gov/sites/brownfields/>)

**Tuesday, January 21, 2014**

**Question:**

What are DDVP pest strips?

**Answer:**

The cited reference points out that Dichlorvos-impregnated resin strips (DDVP pest strips) are among the few organophosphate products still available for indoor residential use. These strips act by inhibiting acetylcholinesterase activity in the brain and nerves of insect pests and are designed to gradually release DDVP vapor for up to 4 months. Acute illnesses in humans associated with nonlethal acute exposures usually resolve completely, but recovery is not always rapid. (MMWR. Notes from the Field: Acute Illness Associated with Use of Pest Strips — Seven U.S. States and Canada, 2000–2013. January 17, 2014 / 63(02); 42-43)

**Monday, January 20, 2014**

**Question:**

What vesicant, produced by beetles belonging to the order Coleoptera, family Meloidae, has been used in the past as an aphrodisiac, an abortifacient and a veterinary diuretic?

**Answer:**

Cantharidin has been used in the past as an aphrodisiac, an abortifacient and a veterinary diuretic. This substance is found in all body fluids of blister beetles. The cited article notes "Cantharidin has a long, infamous reputation for being an aphrodisiac and is known as Spanish fly". This reputation is based on the observation of pelvic congestion in women and priapism in men following cantharidin ingestion. The authors go on to note "Although cantharidin is not a true aphrodisiac, poisonings after surreptitious placement still occur." (Moed L, et al. Cantharidin revisited: A blistering defense of an ancient medicine. 2001 Arch Dermatol 137:1357-1360)

**Friday, January 17, 2014**

**Question:**

What is "Clark I" and what is "Clark II"? What is the primary degradation product of Clark I and Clark II?

**Answer:**

The chemical diphenylchloroarsine is also known as "Clark I" and the chemical diphenylcyanoarsine is also known as "Clark II". According to the cited reference, both of these chemicals were synthesized for the Japanese Imperial Army as "chemical weapons of emetic type under the code name Agent Red No. 1". The authors point out that "During World War II, large amounts of diphenylcyanoarsine and diphenylchloroarsine were manufactured both in the United States and European countries as well as in Japan". Diphenylarsinic acid (DPAA) is the primary degradation product of these chemicals. (Ishii K, et al. Diphenylarsinic acid poisoning from chemical weapons in Kamisu, Japan. 2004 Ann Neurol 56:741–745)

**Thursday, January 16, 2014**

**Question:**

What is kajal?

**Answer:**

Kajal is a lead-containing traditional eye cosmetic that originates from Afghanistan and is often applied to the eyelids of Afgani children. It has been brought to the U.S. by the Afgan immigrant community and thus has been identified as a potential lead hazard for children. Laboratory analysis of this material has been reported to be as high as 70% lead content for this substance. The cited reference notes "Despite the FDA import ban on kohl, surma, and kajal, these products still appear in households, transported in personal luggage and distributed illegally by retailers. The risk for high BLLs caused by repeated exposure to multiple lead-contaminated consumer products and accumulation is a concern." (Childhood Lead Exposure Associated with the Use of Kajal, an Eye Cosmetic from Afghanistan — Albuquerque, New Mexico, 2013. MMWR November 22, 2013 / 62(46); 917-919)

**Wednesday, January 15, 2014**

**Question:**

What is "paraquat tongue"?

**Answer:**

"Paraquat tongue" is seen within a few days of oral ingestion of concentrated paraquat. This manifestation involves ulcerated and bleeding lesion of the tongue. The authors of the cited reference point out that these findings "are of little prognostic significance as they occur even in those who spit paraquat out without swallowing." (Gawarammana IB and Buckley NA. Medical management of paraquat ingestion. 2011 Br J Clin Pharmacol 72(5):745-757)

**Tuesday, January 14, 2014**

**Question:**

What syndrome was first identified in patients after undergoing medical treatment of peptic ulcer disease with milk and what are the clinical characteristics of this syndrome?

**Answer:**

The syndrome at issue is known as milk-alkali syndrome (MAS). The cited article reports "MAS consists of hypercalcemia, varying degrees of renal failure and metabolic alkalosis due to the ingestion of large amounts of calcium and absorbable alkali." (Medarov BI. 2009 Milk-alkali syndrome. 84(3): 261-267)

**Monday, January 13, 2014**

**Question:**

Various studies have looked at college students, police officers, physicians, bartenders, psychologists and alcohol counselors with regard to their ability to diagnose alcohol intoxication. Which of these groups shows consistent ability to diagnose alcohol intoxication without access to specialized tests?

**Answer:**

The cited reference notes "In general, none of these groups show a consistent ability to diagnose (alcohol) intoxication without access to specialized tests." (Rubenzer S. Judging intoxication. 2011 Behav Sci law 29:116-137)



**Friday, January 10, 2014**

**Question:**

What is the first symptom of scorpion envenoming?

**Answer:**

The cited reference notes that localized pain is the first symptom of scorpion envenoming. The authors go on to state, "localized pain reflects the penetration of the venom and is a valuable warning signal, especially in children. Pain is present in more than 95% of cases of envenoming and may be associated with edema and erythema (in 20% of cases), and more rarely small blisters." (Chippaux J. Emerging option for the management of scorpion stings. 2012 Drug Design, Development and Therapy. 6:165-178)

**Thursday, January 9, 2014**

**Question:**

The use of zinc protoporphyrin (ZPP) has fallen out of favor as a screening tool for lead toxicity due its poor sensitivity at lower levels of blood lead, among other reasons. There are specificity issues as well and ZPP may be elevated in a number of other medical conditions. In what medical conditions, not associated with elevated blood lead levels, may ZPP also be elevated?

**Answer:**

ZPP has been reported to be elevated in iron deficiency anemia, sickle cell anemia, sideroblastic anemia, anemia of chronic disease, erythropoietic protoporphyria and vanadium exposure. (Martin CJ et al. The interpretation of zinc protoporphyrin changes in lead intoxication: a case report and review of the literature. 2004 Occupational med 54: 587-591)

**Wednesday, January 8, 2014**

**Question:**

People living near fracking sites have complained of contamination of ground water and drinking water. What chemical has been the focus of concern with regard to water contamination that may be associated with fracking?

**Answer:**

Residents living near fracking sites have complained of methane contamination of ground and drinking water. (Johnson J. Fracking inquiry justified. 2014 Chemical and Engineering News 92(1): 10)

**Tuesday, January 7, 2014**

**Question:**

In late 1989 of number of cases of eosinophil myalgia syndrome (EMS), a medically serious and occasionally fatal condition, were reported to be associated with the use of a particular dietary supplement. What was that supplement?

**Answer:**

Initial reports indicated that the use of tryptophan as a dietary supplement was responsible for the development of EMS. However, it was eventually determined that the development of EMS was not due to tryptophan itself, but rather to contaminants found in this supplement believed to be introduced during the manufacturing process. (Fernstrom JD. Effects and side effects associated with the non-nutritional use of tryptophan by humans. 2012 J Nutr 142:2236S-2244S)

**Monday, January 6, 2014**

**Question:**

What are metal halide and mercury vapor bulbs? What hazards have been recently associated with halide and mercury vapor light bulbs?

**Answer:**

The FDA notes "Metal halide and mercury vapor bulbs are bright, long-lasting sources of light, most often used to light streets, gyms, sports arenas, banks, and stores. The bulbs have an inner quartz tube, containing the mercury vapor discharge, enclosed by an outer glass bulb that filters out harmful short-wavelength UV radiation. If the outer bulb breaks and the inner tube continues to operate unshielded, intense UV radiation is emitted. UV exposure at this level can cause eye and skin burns, as well as blurred or double vision, headaches, and nausea." (<http://www.fda.gov/Radiation-EmittingProducts/RadiationSafety/AlertsandNotices/ucm116540.htm>, accessed January, 2014)

**Friday, January 3, 2014**

**Question:**

Goldenseal (*Hydrastis canadensis*) is a plant native to the eastern United States and sometimes used as an herbal remedy. What are the active components of goldenseal and what are their proposed mechanisms of action?

**Answer:**

The cited reference reports that "Alkaloids, specifically hydrastine and berberine, are reported to be the active components of goldenseal" with berberine being the predominant component. These authors go on to state: "Berberine has apparent antimicrobial activity in humans and has demonstrated anti-tumor and anti-inflammatory activity, neuroprotective and immunomodulatory properties, and the ability to decrease plasma cholesterol in animals and/or in vitro models. The mechanism of actions for berberine, its metabolites, and/or other alkaloids in goldenseal may involve inhibition of enzymes, including CYPs and topoisomerases, and/or effects on cell signaling, receptors, and transporters." (Dunnick JK et al. Investigating the potential for toxicity from long-term use of the herbal products, goldenseal and milk thistle. 2011 Toxicologic Path 39:398-409)

**Thursday, January 2, 2014**

**Question:**

Why is basophilic stippling considered to be an unreliable indicator of lead intoxication?

**Answer:**

The cited reference notes that basophilic stippling is considered to be an unreliable indicator of lead intoxication "largely on the basis of poor specificity, with one study finding it to be present in 27% of consecutive internal medicine patients without lead exposure, but also poor sensitivity when blood lead levels are below 100 µg/dl." (Martin CJ et al. The interpretation of zinc protoporphyrin changes in lead intoxication: a case report and review of the literature. 2004 Occ Med 54:587-591)

**Wednesday, January 1, 2014**

**Question:**

What is Krokodil, what is its primary component chemical, and what are the characteristics of this core chemical?

**Answer:**

known as Crocodile, Krok or Croc, Krokodil is a mixture of several substances with the core component being the chemical desomorphine. Krokodil first emerged in the Russian drug scene in late 2002. Desomorphine is an opioid analogue first synthesized in the US in 1932. This substance reportedly creates a higher dependence profile than morphine with an analgesic potency 8-10 higher than morphine and a more rapid onset of action with a shorter elimination half life. (Gahr M et al. Desomorphine goes “crocodile”. 2012 J Addictive Dis 31:407-412)

**Tuesday, December 31, 2013**

**Question:**

The Union Carbide disaster that took place in Bhopal, India, in December of 1984 reportedly affected more than 80,000 people and involved the release of methyl isocyanate. What were the primary adverse health effects associated with this disaster?

**Answer:**

Mortality: The cited reference discusses both morbidity and mortality issues related to this disaster as follows. “The death toll 1 wk following the accident exceeded 2,500. In November 1989, the Department of Relief and Rehabilitation, Government of Madhya Pradesh, placed the death toll at 3,598, and by 1994 the toll was estimated at 6,000+. Some uncertainty exists regarding the number of deaths because a portion of the population left the city after the accident and never returned. Independent agencies estimate that the number of disaster-related deaths is currently between 15,000 and 20,000. (25,26)

Morbidity: The same reference notes: “Symptom prevalence surveys conducted during the 1988-1990 time frame indicate that morbidity was higher in the exposed areas (26%) than in the control area (18%). Approximately 11% of people experienced 2 or more spells of illness in a 1-yr period. Respiratory, ocular, and gastrointestinal symptoms accounted for most of this morbidity.” (Dhara R and Dhara VR. The Union Carbide disaster in Bhopal: a review of health effects. 2002 Arch Env Health 57(5): 391-404)

**Monday, December 30, 2013**

**Question:**

What are the known human metabolites of TCE (trichloroethylene)?

**Answer:**

Essentially two sets of metabolites have been identified for TCE: the oxidative metabolites: chloral hydrate (CH), trichloroacetic acid (TCA), and dichloroacetic acid and the GSH conjugation metabolites: dichlorovinyl glutathione and dichlorovinyl cysteine (DCVC). It is generally thought that the oxidative metabolites are responsible for any adverse hepatic effects that may occur and the conjugation metabolites are thought to be responsible for any renal effects that might occur. (Chiu WA et al. Human health effects of trichloroethylene: Key findings and scientific issues. 2012 Environmental Health Perspectives 121(3):303-311)

**Friday, December 27, 2013**

**Question:**

What oral effects have been posited to be due to chronic use of khat?

**Answer:**

Periodontal disease, stomatitis and teeth staining have all been reported in individuals who use khat. (Graziani M et al. Khat chewing from the pharmacological point of view: an update. 2008 Substance Use & Misuse 43:762-783)

**Thursday, December 26, 2013**

**Question:**

What are the risk factors for the development of compartment syndrome following snakebite?

**Answer:**

The cited reference notes that the following factors increase the risk for the development of increased intra-compartmental pressures in patients envenomed following snakebite: 1-envenomations of small children; 2-envenomations of digits; 3-application of ice or cold packs; 4-delayed use of antivenin; 5-inadequate dosing of antivenin. (Cumpston KL. Is there a role for fasciotomy in Crotalinae envenomations in North America? 2011 Clin Tox 49:351-365)

**Wednesday, December 25, 2013**

**Question:**

What is the association between maternal use of SSRIs during pregnancy and the development of autism in the offspring?

**Answer:**

The authors of the cited study report “As compared with no use of SSRIs both before and during pregnancy, use during pregnancy was not associated with a significantly increased risk of autism spectrum disorders (fully adjusted rate ratio, 1.20; 95% confidence interval [CI], 0.90 to 1.61)”. (Hviid A et al. Use of selective serotonin reuptake inhibitors during pregnancy and risk of autism. 2013 NEJM 369:2406-2415)

**Tuesday, December 24, 2013**

**Question:**

In the United States today, lethal injection can be imposed by the courts in 37 states and by the federal government and military. What drugs are utilized in the so-called “three drug protocol” for lethal injection executions in the United States today?

**Answer:**

The so-called “three drug protocol” include thiopental, pancuronium bromide, and potassium chloride. (Zimmers TA et al. Lethal injection for execution: Chemical asphyxiation? 2007 PLoS Medicine 4(4):0646-0653)

**Monday, December 23, 2013****Question:**

During the late 1970s and early 1980s a number of outbreaks of menstrual related toxic shock syndrome (MTSS) were reported. What factors were found to be associated with the development of these outbreaks?

**Answer:**

The cited reference notes these episodes were “temporally related to the introduction of tampons containing highly absorbent synthetic materials shortly before the first cases of MTSS were identified. The risk of developing TSS in women who used tampons was found to be proportional to the absorbency of the tampon used. It was subsequently demonstrated experimentally that increase amounts of oxygen present in the vagina in association with the use of ‘superabsorbent’ tampons resulted in optimal conditions for the growth of *S. aureus* and exotoxin production in the lower genital tract.”

The authors go on to point out “Despite recognition of potential risk factors and the implementation of corrective measures, MTSS continues to occur. The risk of developing MTSS in the ‘post-superabsorbent tampon era’ is proportional to: (i) the absorbency of the tampon used, (ii) the time a tampon has been in place (iii) the number of tampons used during menses and (iv) the number of days of tampon use. In addition, MTSS has been reported sporadically in association with other sanitary products such as towels, minipads and sea sponges.” (Murray RJ Recognition and management of *Staphylococcus aureus* toxin-mediated disease. 2005 Int Med J 35:S106-S119

**Friday, December 20, 2013****Question:**

What are the three forms of inorganic arsenic?

**Answer:**

There are 3 inorganic forms of arsenic as follows. These are so-called “red arsenic” (As<sub>4</sub>S<sub>4</sub>, also known as realgar), “yellow arsenic” (As<sub>2</sub>S<sub>3</sub>, also known as orpiment), and “white arsenic” (arsenic trioxide, As<sub>2</sub>O<sub>3</sub>) (Chen SJ et al. From an old remedy to a magic bullet: molecular mechanisms underlying the therapeutic effects of arsenic in fighting leukemia. 2011 Blood 117:6425-6437)

**Thursday, December 19, 2013****Question:**

What is vinyl acetate, what is the primary route of exposure to this chemical for humans, what effects are common at both high and low concentrations and what is the mechanism for these effects?

**Answer:**

Vinyl acetate (VA) is used to make other industrial chemicals (such as polyvinyl acetate polymers and ethylenevinyl acetate copolymers). These other chemicals are used primarily to make glues for the packaging and building industries. They are also used to make paints, textiles, and paper. Most human exposures to VA are via the inhalation route. People who were exposed to vinyl acetate in air for short periods complain of irritation to their eyes, nose, and throat. Volunteers exposed to higher concentrations of vinyl acetate in air report coughing, hoarseness and ocular irritation. The basis for the respiratory irritation is the fact that VA is converted, in vivo, to the irritants acetic acid and acetaldehyde at the site of contact in the upper respiratory tract. (Hengstler JG et al. Challenging dogma: Thresholds for genotoxic carcinogens? The case of vinyl acetate. 2003 Annu Rev Pharmacol Toxicol 43:485-520)

**Wednesday, December 18, 2013****Question:**

How is the chemical nitrogen trichloride generated in swimming pools and what role might this chemical play in the development of pulmonary problems in swimmers and those who work near swimming pools?

**Answer:**

Nitrogen trichloride is formed when organic matter on the body of swimmers comes into contact with chlorinated pool water. It is a strong pulmonary irritant and it is posited that inhalation of this chemical may damage the pulmonary epithelium and increase membrane permeability and may play a role in the development of asthma in swimmers, lifeguards and others who spend time near indoor pools. (Nieuwenhuijsen MJ. The chlorine hypothesis: fact or fiction? 2007 Occup Environ Med 64:6–7.)

**Tuesday, December 17, 2013****Question:**

Prenatal exposure to which anti-epileptic drug carries the highest risk for the development of spina bifida?

**Answer:**

Valproic acid is associated with the highest spina bifida risk. (Nicolai J et al. Neurodevelopmental delay in children exposed to antiepileptic drugs in utero: A critical review directed at structural study-bias. 2008 J Neurological Sci 271:1-14)

**Monday, December 16, 2013****Question:**

Synthetic cannabinoids such as K2, Spice, XLR-11 and others are related to delta-9-tetrahydrocannabinol, the active ingredient in marijuana but important clinical differences have been identified. What are the clinical differences seen associated with acute intoxication with the synthetic cannabinoids as compared with marijuana?

**Answer:**

Synthetic cannabinoids are noted to be up to to three times more likely to manifest sympathomimetic effects (i.e., tachycardia and hypertension), and roughly five times more likely to be associated with hallucinations. An increase in the occurrence of seizures has been reported with synthetic cannabinoid use. In addition, unanticipated acute renal injury has been reported in association with the abuse of synthetic cannabinoids. (Acute Kidney Injury Associated with Synthetic Cannabinoid Use — Multiple States, 2012. Morbidity and Mortality Weekly Report. February 15, 2013 / 62(06); 93-98)

**Friday, December 13, 2013**

**Question:**

Which pigment is most commonly associated with the development of lichenoid and granulomatous reactions in tattoos?

**Answer:**

According to the cited reference, "red pigment from mercuric sulfide (cinnabar) is most commonly associated with lichenoid and granulomatous reactions". (Juhas E and English JC. Tattoo-associated complications. 2013 J Pediatr Adolesc Gynecol 26: 125-129)

**Thursday, December 12, 2013**

**Question:**

What is a so-called "standard drink" and what is the definition of "risk drinking" in terms of consumption of standard drinks?

**Answer:**

A "standard drink" contains 14 g of ethanol and is exemplified by 12 oz of beer, 5 oz of wine, or 1.5 oz of 80-proof liquor. "Risk drinking" is defined as an average of 15 or more standard drinks per week or 5 or more on an occasion for men and 8 or more drinks weekly or 4 or more on an occasion for women and people older than 65 years of age. (Friedmann PD. Alcohol use in adults. 2013 NEJM 368:365-373)

**Wednesday, December 11, 2013**

**Question:**

Granulocyte stimulating factor has been used in healthy individuals who serve as stem cell donors as well as in a wide variety of other individuals. G-CSF has been associated with a variety of adverse effects including headache, malaise, fatigue, nausea and night sweats. Many patients also report bone pain associated with receiving G-CSF. What percent of individuals receiving this medication will experience bone pain?

**Answer:**

According to the cited reference, "Bone pain has been reported in 83 percent of healthy donors given G-CSF, is usually mild to moderate, and usually responds in part to non-steroidal analgesics." (Froberg Mk, et al. Changes in serum osteocalcin and bone-specific alkaline phosphatase are associated with bone pain in donors receiving granulocyte-colony-stimulating factor for peripheral blood stem and progenitor cell collection. 1999 Transfusion 39:410-414)

**Tuesday, December 10, 2013**

**Question:**

What is Otto Fuel II and what are its constituent chemicals?

**Answer:**

Otto Fuel II is a distinct-smelling, reddish-orange, oily liquid that the U.S. Navy uses as a fuel for torpedoes and other weapon systems. It is a mixture of three synthetic substances: propylene glycol dinitrate (the major component), 2-nitrodiphenylamine, and dibutyl sebacate. Propylene glycol dinitrate, a colorless liquid with an unpleasant odor, is explosive. 2-Nitrodiphenylamine is an orange solid used to control the explosion of propylene glycol dinitrate. Dibutyl sebacate is a clear liquid used for making plastics, many of which are used for food packaging. It is also used to enhance flavor in some foods such as ice cream, candy, baked goods, and nonalcoholic drinks, and is found in some shaving creams. (<http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=152>)

**Monday, December 9, 2013**

**Question:**

What generally unavoidable ocular complication of radiation results following orbital radiation exposure and/or following total body irradiation prior to bone marrow transplantation?

**Answer:**

Ocular cataracts often result following orbital radiation exposure or following total body irradiation prior to bone marrow transplantation. (Dymlach JR et al. Effect of estrogen on radiation-induced cataractogenesis. 2006 Rad Research 165:9-15)

**Friday, December 6, 2013**

**Question:**

What is endosulfan and what is the primary target organ for the toxicity of this chemical?

**Answer:**

Endosulfan is a restricted-use pesticide effective against aphids, fruit worms, beetles, leafhoppers, moth larvae, and white flies on a wide variety of crops. It is not approved for residential use. It is sold as a mixture of two different forms of the same chemical (referred to as  $\alpha$ - and  $\beta$ -endosulfan). It is a cream-to- brown-colored solid that may appear crystalline or in flakes. It has a distinct odor similar to turpentine. The use of endosulfan is being restricted to certain crops and is scheduled to be eliminated for all uses by 2016. The main target of endosulfan in humans and animals is the nervous system. Exposure to high amounts of endosulfan by any route produces over-stimulation of the central nervous system resulting in hyperactivity, tremors, decreased respiration, dyspnea, salivation, tonic-clonic convulsions, and death. (accessed at: <http://www.atsdr.cdc.gov/toxprofiles/tp41.pdf>)

**Thursday, December 5, 2013**

**Question:**

A "cock-walk" gait (also called "coq au pied") has been associated in the literature with extreme (high dose/ long duration) exposure to what heavy metal?

**Answer:**

The so-called "cock-walk" gait has been described in association with manganese-induced neurotoxicity that may arise in association with extreme exposures to this metal. (Olanow CW. Manganese induced parkinsonism and Parkinson's Disease. 2004 Ann NY Acad Sci 1021:209-223)

**Wednesday, December 4, 2013**

**Question:**

In 1954, Case and Hosker reported a 200-fold increased risk for what form of cancer in English and Welsh workers exposed to 2-naphthylamine?

**Answer:**

In 1954, Case and Hosker reported a 200-fold increased risk bladder cancer in English and Welsh workers exposed to 2-naphthylamine. (Case RAM and Hosker ME: Tumours of the urinary bladder as an occupational disease in the rubber industry in England and Wales. 1954 Br J Prev Soc Med 8:39-50)

**Tuesday, December 3, 2013**

**Question:**

Which potential bio-terrorism agent is associated with the development of hemorrhagic mediastinitis?

**Answer:**

The authors of the cited article note "Inhalational anthrax is caused by inhalation and alveolar deposition of spores less than 5 mm in size. Spores are phagocytosed by macrophages and carried to local mediastinal lymph nodes where they germinate into vegetative forms, replicate, and produce hemorrhagic mediastinitis." (Sweeney D et al. Anthrax infection. 2011 Amer J Resp Crit Care Med 184(12):1334-1341)

**Monday, December 2, 2013**

**Question:**

The combination of which two drugs was at issue in the now infamous case involving Libby Zion?

**Answer:**

The Libby Zion case reportedly involved the ill-advised combination of meperidine and phenelzine with the precipitation of a fatal serotonin syndrome (although some have suggested that cocaine and/or other drugs may also have been involved). (Asch DA and Parker RM. The Libby Zion Case. One step forward or two steps backward? 1988 NEJM 318(12): 771-775)

**Friday, November 29, 2013**

**Question:**

The chemical bis(chloromethyl) ether has been posited to cause cancer in some workers who have been exposed to this chemical under certain circumstances. In fact, EPA classifies this chemical as a Group A carcinogen and IARC classifies it as a Group 1 carcinogen. Cancer of what organ may be associated with exposure to bis(chloromethyl) ether in some settings?

**Answer:**

The ATSDR reports that a number of case studies and epidemiological studies of occupationally-exposed workers indicate that inhalation of BCME or CME (chloromethyl ether) containing BCME is associated with increased risk of lung cancer. (accessed at <http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=919&tid=188>)

**Thursday, November 28, 2013**

**Question:**

What blood lead level is currently designated by the CDC as "elevated" for adults?

**Answer:**

CDC has designated 10 µg/dL as the reference BLL for adults; levels ≥10 µg/dL are considered elevated. (CDC. Adult Blood Lead Epidemiology and Surveillance (ABLES). Cincinnati, OH: US Department of Health and Human Services, CDC, National Institute for Occupational Safety and Health; 2013. Available at <http://www.cdc.gov/niosh/topics/ables/description.html>.)

**Wednesday, November 27, 2013**

**Question:**

Libby, Montana, is the site of an important toxicological issue that has garnered much notoriety over the years. What substances are involved in the well-known toxicological issues that emanated from Libby, Montana?

**Answer:**

Vermiculite mining in and near the town of Libby, Montana, began in the 1920s and was continued by the W.R. Grace Company from 1963 until 1990. The vermiculite ore mined in Libby was contaminated with tremolite asbestos. In 1999, The Agency for Toxic Substances and Disease Registry (ATSDR) was asked by the Department of Health and Human Services (DHHS) to evaluate human health concerns in Libby that were related to asbestos exposure. Since that time, ATSDR has worked closely with the community on a number of projects and activities, including a recently announced five year initiative to examine the health effects of exposure to Libby amphibole asbestos.

**Tuesday, November 26, 2013**

**Question:**

Measurement of what analyte in blood, tissue and/or urine has been used to confirm exposure to hydrogen sulfide?

**Answer:**

Measurement of thiosulfate in blood, tissue and/or urine has been used, with variable results, to confirm exposure to hydrogen sulfide. (Policastro MA and Otten EJ. Case Files of the University of Cincinnati Fellowship in Medical Toxicology: Two patients with acute lethal occupational exposure to hydrogen sulfide. 2007 J Med Tox 3(2): 73-81)

**Monday, November 25, 2013**

**Question:**

What is the most accurate biomarker of toluene exposure? Which toluene metabolites are sometimes also used to determine workplace exposure to toluene?

**Answer:**

The most accurate biomarker of toluene exposure is the presence of toluene in the blood or serum but measurements of metabolites in the urine are sometimes preferred as urine sampling is less invasive. The cited resource notes “Although measurement of urinary excretion of toluene metabolites (hippuric acid, mercapturic acids, ortho-cresol and para-cresol) is a less invasive method than blood sampling for determining toluene exposure, the presence of these compounds in the urine is not definitive proof of toluene exposure since they are also produced by metabolism from the normal diet.” (accessed at <http://www.atsdr.cdc.gov/toxprofiles/tp56-c2.pdf>)

**Friday, November 22, 2013**

**Question:**

What toxicity may result from the ingestion of the common milkweed plant (*Asclepias syriaca*)?

**Answer:**

Cardio-active steroid toxicity may result from the ingestion of the common milkweed plant (*Asclepias syriaca*). The authors of the cited article note that this plant may contain the cardio-active steroids asclepiadin, gomphoside and afroside. (Simpson NS et al. What toxicity may result from ingestion of the plant pictured below? Answer: Cardioactive steroid toxicity from common milkweed. 2013 J Med Toxicol 9(3):287-288)

**Thursday, November 21, 2013**

**Question:**

What percentage of adult smokers who try to quit with the help of nicotine-containing electronic cigarettes actually achieve abstinence after six months of use and how does that compare with those using the nicotine patch or a placebo device?

**Answer:**

According to the cited reference “The percentage of patients who achieved abstinence from smoking tobacco cigarettes at 6 months was slightly higher with the nicotine e-cigarettes (7.3%) than with the nicotine patch (5.8%) or placebo device (4.1%); these differences were not statistically significant. (Bullen C et al. Electronic cigarettes for smoking cessation: a randomized controlled trial. 2013 Lancet September 9 2013 (epub) as cited in The Medical Letter November 11, 2013, 55(1429):89)

**Wednesday, November 20, 2013**

**Question:**

What characterizes the peripheral neuropathy reported to be associated with fluoroquinolones?

**Answer:**

According to the cited reference the peripheral neuropathy associated with fluoroquinolones often starts within just a few days of beginning therapy with these drugs and may, in some cases, be permanent. The reference reports this peripheral neuropathy is characterized by “pain, tingling, burning, numbness, weakness and change in sensation to touch, pain, and temperature in the extremities”. (The Medical Letter November 11, 2013, 55(1429):89)

**Tuesday, November 19, 2013**

**Question:**

What is RDX?

**Answer:**

“RDX”, also known as cyclonite, stands for Royal Demolition explosive. It is also known as cyclonite or hexogen. The chemical name for RDX is 1,3,5-trinitro-1,3,5-triazine. It is a white powder and is very explosive. RDX is used as an explosive and is also used in combination with other ingredients in explosives. C-4 explosive is approximately 91% RDX. Its odor and taste are unknown. It is a synthetic product that does not occur naturally in the environment. It creates fumes when it is burned with other substances. Limited studies have shown adverse gastrointestinal, hematological, hepatic, and renal effects in workers exposed to C-4 (an explosive composed of 91% RDX) or RDX dusts via inhalation. (accessed at <http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=72>)

**Monday, November 18, 2013**

**Question:**

What is “surgical smoke” and what are the primary risks of exposure to this material for workers who might be exposed to surgical smoke?

**Answer:**

The cited reference notes that surgical smoke is “the gaseous by-product produced when tissue is dissected or cauterized by heat generating devices such as lasers, electrosurgical units, ultrasonic devices and high speed burs, drills and saws.” The author states “The main risks to the health of perioperative personnel from surgical smoke are acute and chronic respiratory irritation and inflammation, irritation of the eyes and skin, transmission of infection, and genotoxicity by its mutagenic properties”. However, the author concludes “Due to the nature of this topic there is no definite proven link between surgical smoke and the effect it has on human health, but neither is there any firm evidence that shows it is safe to be exposed to surgical smoke. Therefore it would seem that until such time as evidence shows that surgical smoke poses no risks to health, a preventative approach would be the sensible option.” (Sanderson C. Surgical smoke. 2012 J Perioperative Prac 22(4): 122-128)

**Friday, November 15, 2013**

**Question:**

It is thought that benzene may metabolize into 13 or more compounds. Which of these may be detected in human urine and which one has been used as a means to monitor workers with potential benzene exposure?

**Answer:**

Benzene metabolites phenol, muconic acid and S-phenylmercapturic acid can be measured in the urine. Phenol has been used to check for benzene exposure in workers. (ATSDR Toxicological Profile for Benzene. August 2007, access at <http://www.atsdr.cdc.gov/toxprofiles/tp3.pdf>)

**Thursday, November 14, 2013****Question:**

What is the only currently approved non-stimulant drug for adult ADHD?

**Answer:**

Atomoxetine (Strattera) is the only currently approved non-stimulant drug for adult ADHD. The authors of the cited paper note that "Atomoxetine is a blocker of norepinephrine transporters that enhances noradrenergic signaling in the brain and dopaminergic signaling in the frontal cortex, since in this brain region, norepinephrine transporters also remove dopamine." (Volkow ND and Swanson JM. Adult attention deficit-hyperactivity disorder. 2013 NEJM 369:1935-1944)

**Wednesday, November 13, 2013****Question:**

What is the pathophysiology of ACE-inhibitor associated angioedema?

**Answer:**

The cited reference notes that the exact pathophysiology of ACE-inhibitor angioedema is considered to be controversial. However, the authors point out that conventional wisdom believes decreased degradation of bradykinin (a strong vasodilator capable of increasing blood vessel permeability) is the primary pathophysiologic process for ACE-inhibitor angioedema. They go on to point out that "C1-inhibitor abnormalities, carboxyalkyl dipeptide N, urinary kallikrein and inflammatory mediators such as interleukin-1 and tumor necrosis factor have also been proposed as mediators for ACE-inhibitor angioedema". (Winters ME et al. Emergency department management of patients with ACE-inhibitor angioedema. 2013 J Emerg Med 45(5): 775-780)

**Tuesday, November 12, 2013****Question:**

Methotrexate has been implicated in the development of optic neuropathy. What is the mechanism for this effect?

**Answer:**

Methotrexate, in combination with dietary deficiency, may result in decreased folate levels in the serum. Low serum folate levels in turn may result in an elevation of plasma homocysteine levels. The cited reference notes "Elevated homocysteine levels may lead to inhibition of neuronal mitochondrial function by inducing reactive oxygen species and ultimately results in neuro-degeneration." They go on to point out "The metabolically active papillomacular bundle could be affected preferentially producing profound bilateral loss of visual acuity and field defects similar to those seen in hereditary optic neuropathies." (Clare G et al. Reversible optic neuropathy associated with low-dose methotrexate therapy. 2005 J Neuro-Ophthalmol 25(2): 109-112)

**Monday, November 11, 2013****Question:**

What is the primary route for exposure to styrene by the US populations? What industries likely have the highest potential for exposure to this chemical?

**Answer:**

The primary route of styrene exposure is via inhalation of contaminated indoor air. The industries with the highest potential exposure are probably the reinforced plastics factories, boatbuilding facilities, and polystyrene factories. (ATSDR Toxicological Profiles for Styrene, accessed November, 2013 at <http://www.atsdr.cdc.gov/toxprofiles/tp53-c6.pdf>)

**Friday, November 8, 2013****Question:**

"SILENT", or the "Syndrome of Irreversible Lithium-Effectuated Neurotoxicity", involves persisting neurologic sequelae associated with lithium carbonate. What doses of lithium are most likely to cause SILENT?

**Answer:**

The authors of the cited reference note that "SILENT occurs even at therapeutic doses of the drug. From our review of cases, the doses responsible for SILENT ranged from as low as 438 mg/day to as high as 8100 mg/day." (Munshi K et al. The syndrome of irreversible lithium-effectuated neurotoxicity. 2005 Clin Neuropharmacol 28:38-49)

**Thursday, November 7, 2013****Question:**

What are the early skin findings associated with thallium poisoning?

**Answer:**

The early skin findings associated with thallium poisoning have been described as erythematous lesions on the cheeks and in the perioral region in the first week following thallium poisoning. These lesions usually go on to develop into acneiform or pustular eruptions. (Lu, C et al. Short-term thallium intoxication- Dermatological findings correlated with thallium concentration. 2007 Arch Dermatol 143:93-98)

**Wednesday, November 6, 2013****Question:**

Approximately 10-25% of all lung cancers occur in individuals who have never smoked tobacco products. Which three environmentally available chemicals may play a role in lung tumorigenesis in these "never smokers"?

**Answer:**

Arsenic, asbestos and radon are three prominent carcinogens that may play a role in the development of lung cancer in some individuals with lung cancer who have never smoked. (Hubaux R et al. Arsenic, asbestos and radon: emerging players in lung tumorigenesis. 2012 Env Health 11:89:1-12)

**Tuesday, November 5, 2013****Question:**

What is the mechanism by which the anti-epileptic drug topiramate may increase the risk for renal stones and fractures?

**Answer:**

According to the cited reference, topiramate is a carbonic anhydrase inhibitor that may cause metabolic acidosis. This increases the risk for fractures and renal stones. Consequently the drug manufacturer recommends that serum bicarbonate be monitored periodically for those individuals taking this drug. (The Medical Letter October 28,2013, 55(1428): 87-88)

**Monday, November 4, 2013****Question:**

Fingolimod (Gilyena) is a sphingosine-1-phosphate receptor modulator and is the first US Food and Drug Administration (FDA)–approved oral agent for the treatment of relapsing forms of multiple sclerosis (MS). What reversible ocular toxicity has been associated with the use of this drug?

**Answer:**

Fingolimod-associated macular edema (FAME) is a dose- dependent toxicity associated with fingolimod therapy. The authors of the cited reference report that this drug associated macular edema typically re-solves upon cessation of therapy (Jain N and Bhatti MT. Fingolimod-associated macular edema: incidence, detection and management. 2012 Neurology 78:672-680)

**Friday, November 1, 2013****Question:**

What is the most serious potential adverse neurologic effect associated with acute inhalational exposure to high concentrations of the chemical ethylbenzene in the occupational setting?

**Answer:**

The most serious potential adverse neurologic effect associated with acute inhalational exposure to high concentrations of the chemical ethylbenzene in the occupational setting is hearing loss. The authors of the cited reference note “This hearing loss is characterized by deterioration in auditory thresholds and alterations in cochlear morphology.” (Zhang M et al. Ethylbenzene-induced hearing loss, neurobehavioral function and neurotransmitter alterations in petrochemical workers. 2013 JOEM 55(9): 1001-1006)

**Thursday, October 31, 2013****Question:**

What nonselective bipyridyl contact herbicide is structurally similar to paraquat though not as widely used in agriculture?

**Answer:**

Diquat (1,1-ethylene-2,2 bipyridilium).( Jones GM and Vale A. Mechanisms of toxicity, clinical features, and management of diquat poisoning: A review. 2000 Clin Tox 38(2):123-128)

**Wednesday, October 30, 2013****Question:**

Paraquat is a herbicide that is widely used in many countries. This chemical has been responsible for a large number of both accidental and intentional poisoning deaths. What are the primary organs targeted by this toxicant?

**Answer:**

The kidneys and the lungs are the primary organs targeted following ingestion of paraquat. (Wunnapuk K et al. Renal biomarkers predict nephrotoxicity after paraquat. 2013 Tox Letters 222:280-288)

**Tuesday, October 29, 2013****Question:**

The artemisinins are a class of antimalarial agents originally developed in China in the 1960s (e.g. artesunate, artemether, artemotil, and dihydro- artemisinin). What forms of toxicity related to the artemisinins are of most clinical concern?

**Answer:**

The potential for the development of neurotoxicity as well as the potential for embryotoxic effects are of concern with regard to the artemisinins. While these toxicities have not been proven, case reports and animal data suggest that neurotoxicity and embryotoxicity may be important. (Rosenthal PJ. Artesunate for the treatment of severe falciparum malaria. 2008 NEJM 358:1829-1836)

**Monday, October 28, 2013****Question:**

What is alimentary toxic aleukia? What are the clinical characteristics of this disorder and exposure to what toxin is believed to cause this syndrome in humans?

**Answer:**

Alimentary toxic aleukia (ATA), a frequently fatal mycotoxicosis, follows the ingestion of overwintered grain or grain by-products infested with fungi. In humans, ATA is characterized by fever, leukopenia and agranulocytosis, as well as bone marrow failure manifested by widespread hemorrhagic sequelae. ATA is thought to be caused by the ingestion of T-2 mycotoxin. (Lutsky II and Mor N. Alimentary toxic aleukia 1981 Am J Pathol 104(2): 189-191)

**Friday, October 25, 2013**



**Question:**

What are the generally accepted principles for opioid detoxification? How long does traditional medically supervised detoxification take? How effective is detoxification by itself on long-term abstinence?

**Answer:**

According to a recent discussion of the topic in the CDC's Mortality Morbidity Weekly Report "Opioid detoxification refers to the discontinuation of opioid use under medical supervision and includes prescribing or administering medications to decrease withdrawal symptoms. Standard detoxification methods include administering gradually reduced doses of long-acting opioid agonists during a 3–21 day period or discontinuing opioids and administering nonopioid medications to block withdrawal symptoms. These methods ameliorate withdrawal symptoms and carry <1% risk for serious adverse events. The effect of detoxification on long-term abstinence is negligible without the addition of longer term evidence-based substance abuse treatment." (September 27, 2013 MMWR 62(38):777-780)

**Thursday, October 24, 2013**

**Question:**

What are so-called "red tides"? What toxins have been associated with "red tides" and what human health effects have reportedly resulted from inhalational exposure to red tides?

**Answer:**

"Red tides" are the manifestation of so-called oceanic "harmful algal blooms" and are caused by dinoflagellates that produce brevetoxins which are potent neurological toxins. The cited reference notes "Exposure to seafood contaminated by brevetoxins is associated with neurotoxic shellfish poisoning in humans and the inhalation of aerosols containing these toxins has been reported to cause various degrees of respiratory irritation as well as asthma." (Fleming LE et al. Exposure and effect assessment of aerosolized red tide toxins and asthma. 2009 Env Health Perspectives 117:1095-1100)

**Wednesday, October 23, 2013**

**Question:**

What is the effect of storing lorazepam or adrenaline hydrochloride at other than recommended storage temperatures such as might occur in EMS vehicles?

**Answer:**

One recent study reported that when stored at room temperature or in a transport vehicle, lorazepam became unstable within a period of weeks while adrenaline hydrochloride remained stable for several months. The authors concluded that the degree of change to various drugs stored in emergency transport vehicles is highly variable. (DeWinter S et al. Impact of temperature exposure on stability if drugs in a real-world out of hospital setting. 2013 Ann Emerg Med 62(4):380-387)

**Tuesday, October 22, 2013**

**Question:**

What percentage of patients receiving unfractionated heparin for post operative antithrombotic prophylaxis may be expected to develop heparin induced thrombocytopenia (HIT)?

**Answer:**

The authors of the cited reference note "HIT occurs in up to 1% of patients receiving unfractionated heparin for postoperative antithrombotic prophylaxis, most frequently in orthopedic patients (4.8%) and more often with unfractionated heparin (4.8%) than with low molecular weight heparin (0.6%)" (Rosenberger LH et al. Bilateral adrenal hemorrhage: The unrecognized cause of hemodynamic collapse associated with heparin-induced thrombocytopenia. 2011 Crit Care Med 39(4):833-838)

**Monday, October 21, 2013**

**Question:**

What is kuchla?

**Answer:**

The strychnine-containing tree *Strychnos nux-vomica* is also known as "kuchla". This plant contains both major and minor alkaloids including strychnine alkaloids and related alkaloids. (Bhati R et al. *Strychnos nux-vomica* seeds: Pharmacognostical standardization, extraction, and antidiabetic activity. 2012 J Ayurveda Integr Med 3(2): 80-84)

**Friday, October 18, 2013**

**Question:**

What are the differences in effects on lung function due to cannabis smoking compared with tobacco smoking?

**Answer:**

The authors performed a population based cohort study (n=1037) of the problem. These authors report "Cannabis appears to have different effects on lung function from those of tobacco. Cannabis use was associated with higher lung volumes, suggesting hyperinflation and increased large-airways resistance, but there was little evidence for airflow obstruction or impairment of gas transfer." (Hancox RJ et al. Effects of cannabis on lung function: a population-based cohort study. 2010 Eur Respir J 35:42-47)

**Thursday, October 17, 2013**

**Question:**

Which chemical is sometimes added to pyrethrin insecticides to increase efficacy of the insecticide?

**Answer:**

Piperonyl butoxide is sometimes added to synergize pyrethrins. (Nayak M. Potential of piperonyl butoxide-synergised pyrethrins against psocids (Psocoptera: Liposcelidae) for stored-grain protection. 2010 Pest Manag Sci 66:295-300)

**Wednesday, October 16, 2013**

**Question:**

Black widow antivenin has been recommended by some authors to be an effective treatment modality for individuals envenomated by this spider. What positive (and negative) clinical effects have been reported after the administration of this antivenin?

**Answer:**

The authors of the cited reference note that “Black widow specific antivenin appears to shorten duration of symptoms and reduce hospitalization more than symptomatic treatment, but can cause allergic reactions including anaphylaxis and death from acute and delayed serum reactions.” (Prongay R and Kelsberg G. Which treatments relieve painful muscle spasms from a black widow spider bite? 2012 J Fam Prac 61(11): 694-695)

**Tuesday, October 15, 2013**

**Question:**

What is the basis of the frequently encountered adverse drug-drug interaction reported between amiodarone and the vitamin K antagonist warfarin?

**Answer:**

Warfarin is a mixture of 2 optically active isomers (R and S enantiomers). The authors of the cited reference point out that “the S enantiomer is approximately 3 times more potent than the R enantiomer and is metabolized primarily by CYP2C9. Inhibition of CYP2C9 by amiodarone and its major metabolite potentiates the anticoagulant effects of warfarin, increasing the risk of serious bleeding.” (Shirolkar SC et al. Dronedarone and vitamin K antagonists: A review of drug-drug interactions. 2010 Am Heart J 160:577-582)

**Monday, October 14, 2013**

**Question:**

Chronic beryllium disease (CBD) is generally considered to be a disorder mediated by cellular and molecular components of the innate and acquired immune systems occurring principally in beryllium-exposed industry workers. What is the current treatment for CBD?

**Answer:**

The cited reference points out that there is no cure for CBD. However these authors recommend “Treatment focuses on control of inflammation and immune reactions although studies show that beryllium can persist in CBD granuloma for decades after the last Be exposure. Prednisone is administered when there is evidence of pulmonary impairment based on symptoms, pulmonary function tests and exercise testing. Corticosteroids are required life-long with other supportive treatment such as oxygen therapy for those with hypoxemia and/or pulmonary hypertension. Methotrexate may be used in patients that do not respond to steroids. Steroid treatment has been associated with improvement in lung function in CBD patients, suppressing lung granuloma formation and inhibiting progression to pulmonary fibrosis in some patients.” (Sawyer RT and Maier LA. Chronic beryllium disease: an updated model interaction between innate and acquired immunity. 2011 Biometals 24;1-17)

**Friday, October 11, 2013**

**Question:**

Drug- and herb-induced hepatotoxicity have been reported in association with exposure to a variety of drugs and herbs used as dietary supplements. These can lead to severe acute hepatitis and liver failure. Within the past few days, a number of cases of acute hepatitis and liver failure have been reported in association with ingestion of a dietary supplement intended for weight loss or muscle building. What supplement is the subject of these ongoing cases?

**Answer:**

The supplement at issue is “OxyElite Pro” which has recently been “voluntarily recalled” nationwide in the US. Some iterations of this supplement contain DMAA (dimethylamylamine) and this chemical is the current target of investigations for the cases mentioned above. (Park SY et al. Acute hepatitis and liver failure following the use of a dietary supplement intended for weight loss or muscle building — May–October 2013. MMWR, October 11, 2013, 62(40))

**Thursday, October 10, 2013**

**Question:**

Nickel carbonyl or nickel tetracarbonyl, is a potentially harmful, colorless, volatile, and flammable liquid formed when carbon monoxide contacts nickel. What are the industrial uses for nickel carbonyl?

**Answer:**

The cited reference notes that “Nickel carbonyl is used in the extraction of nickel (Mond process), gas plating, and as a catalyst and reactant in chemical synthesis, and is usually encountered as a vapor that is rapidly absorbed after inhalation.” (Gan SI, et al. Inhalational nickel carbonyl poisoning in waste processing workers. 2005 Chest 128:424-429)

**Wednesday, October 9, 2013**

**Question:**

What are the pathological findings associated with fatal lindane toxicity?

**Answer:**

Post mortem examinations of cases of fatal lindane toxicity report “fatty infiltration of the liver, degeneration of cardiac muscle, and necrosis of vessels of lungs, kidneys, and brain”. (Solomon LM et al. Gamma benzene hexachloride toxicity: a review. 1977 Arch Dermatol 113:353–357 as cited in Singal A and Thami G. Lindane neurotoxicity in childhood 2006 Am J Ther 13:277-280)

**Tuesday, October 8, 2013**

**Question:**

What is TSCA?

**Answer:**

TSCA stands for the Toxic Substances Control Act of 1976. This act provides EPA with authority to require reporting, record-keeping and testing requirements, and restrictions relating to chemical substances and/or mixtures. Certain substances are generally excluded from TSCA, including, among others, food, drugs, cosmetics and pesticides. TSCA addresses the production, importation, use, and disposal of specific chemicals including polychlorinated biphenyls (PCBs), asbestos, radon and lead-based paint. (<http://www2.epa.gov/laws-regulations/summary-toxic-substances-control-act>)

**Monday, October 7, 2013**

**Question:**

What is Compound 1080, what is it used for, and what is the mechanism of action?

**Answer:**

The chemical name for compound 1080 is sodium monofluoroacetate, although it is commonly known as 1080. While the use of this chemical is country specific, this material is currently used in the USA (although it has been banned for use in a number of states) with use restricted to a livestock-protection collar to protect sheep and cattle from coyotes. The cited reference notes "1080 is converted within the animal to fluorocitrate, which inhibits the energy production in the tricarboxylic acid (Krebs) cycle. This results in accumulation of citrate in the tissues and blood, energy deprivation, and death." (Eason C. Sodium monofluoroacetate (1080) risk assessment and risk communication. 2002 Toxicology 181-182:523-530)

**Friday, October 4, 2013**

**Question:**

What is the most widely used biomarker for estimating both active and passive exposure to tobacco smoke?

**Answer:**

Urine cotinine levels are the most widely used biomarker for estimating both active and passive exposure to tobacco smoke. The cited reference notes: "Cotinine, which is a major metabolite of nicotine is stable in body fluids, has a long half-life, low plasma protein binding (2.6%), and dose independent disposition kinetics. These factors make cotinine a good marker for estimating both active and passive exposure to tobacco smoke." (Behera D, et al. Urinary levels of nicotine and cotinine in tobacco users. 2003 Indian J med Res 118:129-133)

**Thursday, October 3, 2013**

**Question:**

Para-phenylenediamine (PPD) is often added to henna temporary tattoo solutions in order to decrease application time and to intensify the color. What clinical complications may be associated with the presence of PPD in henna tattoos?

**Answer:**

The authors of the cited reference indicate that PPD "is responsible for most of the complications reported after henna tattoos: localized or generalized contact dermatitis, hypertrophic or keloid scars, and temporary or permanent hyper- or hypopigmentation. More rarely, type I hypersensitivity reactions (urticaria, angioedema, or anaphylaxis) with potentially lethal outcomes have been reported." (Kluger N et al. Tatouages temporaires au henné: des effets indésirables parfois graves. 2008 Presse Med 37:1138-1142)

**Wednesday, October 2, 2013**

**Question:**

What are so-called "asbestos bodies" and what is their clinical significance?

**Answer:**

The cited reference notes that asbestos bodies are "inhaled asbestos fibers that have been coated with hemosiderin by alveolar macrophages. Asbestos bodies in bronchoalveolar lavage fluid may be reliable markers of asbestos exposure, and can be present as early as 10 months after exposure." (Vathesatogkit P, et al. Clinical correlation of asbestos bodies in BAL fluid. 2004 Chest 126:966-971)

**Tuesday, October 1, 2013**

**Question:**

Quinolone antibiotics are associated with an increased risk for the development of tendinopathies. What sub-groups of patients are more prone to develop quinolone-associated tendinopathies?

**Answer:**

The risk for quinolone-associated tendinopathy is more pronounced in elderly patients, non-obese patients and those patients who are concurrently taking glucocorticoid medications. In addition, females, diabetics, and renal failure patients may be at increased risk for quinolone-associated Achilles tendonitis while females are at increased risk for quinolone-associated tendon rupture. (Wise BL et al. Impact of age, sex, obesity and steroid use on quinolone-associated tendon disorders. 2012 Am J Med 125(12): 1228.e23-1228.e28)

**Monday, September 30, 2013**

**Question:**

Cephalosporin-induced neurotoxicity may be manifest by a variety of clinical findings including acutely altered mental status, myoclonus, asterixis, seizures, nonconvulsive status epilepticus, and coma. Which sub-group of patients are at higher risk for the development of cephalosporin-induced neurotoxicity and what is the most likely mechanism for the development of cephalosporin-induced neurotoxicity?

**Answer:**

The cited reference notes "Patients who are elderly, those with renal insufficiency, and those with prior neurologic disease may be particularly prone to the neurotoxic effects." The authors go on to state "The main mechanism of neurotoxicity appears to involve gamma-aminobutyric acid A receptor inhibition, although other mechanisms may be possible." (Grill MF and Magenti R. Cephalosporin-induced neurotoxicity: clinical manifestations, potential pathogenic mechanisms, and the role of electroencephalographic monitoring. 2008 Ann Pharmacother 42(12):1843-1850)

**Friday, September 27, 2013**

**Question:**

Why are ingested lithium ion batteries associated with a proportionally greater number of significant outcomes when compared with batteries containing other electrolytes?

**Answer:**

The cited article points out that 1- Lithium ion batteries tend to be larger and thus more readily become impacted in the pharynx or esophagus; 2-lithium ion batteries generate a higher voltage in the range of 3.6 volts. (Dawe N et al. Unwitnessed lithium ion disc battery ingestion: case report and review of best practice management of an increasing clinical concern. 2013 J Laryngology Oto 127:84-87)

**Thursday, September 26, 2013****Question:**

What is the mechanism for the development of clinical ergotism in individuals who may be taking antiretroviral agents in conjunction with ergotamine?

**Answer:**

Ergotamines are substrates of the cytochrome P450 3A4 isozyme. Certain antiretroviral drugs (e.g. amprenavir, darunavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir and tipranavir) are potent CYP 3A4 inhibitors and thus, when taken in concert with ergotamines a marked increase in ergotamine levels in the blood can occur and may therefore induce clinical ergotism. (Frohlich G. et al. Holy fire in an HIV positive man: a case of 21st century ergotism. 2010 CMAJ 182(4): 378-380)

**Wednesday, September 25, 2013****Question:**

Oral fluconazole exposure during pregnancy is associated with the development of what cardiac abnormality?

**Answer:**

While not associated with a significant increased risk of birth defects in general, oral fluconazole exposure during pregnancy is associated with an increased risk for the development of tetralogy of Fallot. The cited reference reports a significantly increased risk of tetralogy of Fallot with an adjusted odds ratio of 3.16 (95% CI, 1.49 to 6.71) in fluconazole-exposed pregnancies. (Molgaard-Nielsen D et al. Use of oral fluconazole during pregnancy and the risk of birth defects. 2013 NEJM 369(9): 830-839)

**Tuesday, September 24, 2013****Question:**

What is the cellular thermal shift assay (CETSA)?

**Answer:**

According to the cited reference, CETSA is “A new label free strategy (one that uses the native drug without requiring chemical tagging or modification)” devised to measure “drug-target binding inside cells, facilitating the studies of variables such as drug transport, activation, tissue distribution, target specificity and resistance.” This technique allows researchers to assess effective drug targeting within cells. The author of the cited article points out “Given that the majority of drugs fail in clinical trials and in the clinic owing to unforeseen toxicity and lack of efficacy, the further development of CETSA and related methods may auger well for the development of safe and effective therapeutic agents.” (Huang J. Tracking drugs. 2013 NEJM 369(12): 1168-1169)

**Friday, September 20, 2013****Question:**

Controversy exists with regard to the role benzene exposure may play in the development of certain hematologic cancers while most authorities are clear with regard to high concentration exposure to benzene being causative of acute myelogenous leukemia (AML). Recently discussions regarding the risk of low level exposures to benzene have intensified. What is the relationship between low level benzene exposure and the development of either AML (acute myelogenous leukemia) or myelodysplastic syndrome (MDS)?

**Answer:**

One recent study looked at low levels of benzene exposure for petroleum workers. This industry funded study concluded: “Relatively low-level exposure to benzene experienced by petroleum distribution workers was associated with an increased risk of MDS, but not AML, suggesting that MDS may be the more relevant health risk for lower exposures.” (Schnatter AR et al. Myelodysplastic syndrome and benzene exposure among petroleum workers: An international pooled analysis. 2012 J Natl Cancer Inst 104:1724-1737)

**Thursday, September 19, 2013****Question:**

Which botanical medicine, first used by Native Americans, contains the alkaloid berberine, an antimicrobial with activity against Chlamydia trachomatis (as well as other organisms)?

**Answer:**

Goldenseal root contains berberine and was first used by members of the Cherokee nation to treat eye and skin infections and by the Iroquois for GI illnesses. (Junio HA et al. Synergy directed fractionation of botanical medicine: A case study with Goldenseal (Hydrastis Canadensis) 2011 J Nat Prod 74:1621-1629)

**Wednesday, September 18, 2013****Question:**

What is the typical neuropathological finding demonstrable on neuroimaging that is associated with methanol poisoning?

**Answer:**

Necrosis of the putamen is the typical neuropathological finding demonstrable on neuroimaging that is associated with methanol poisoning. (Anderson C et al MRI enhancing brain lesions in methanol intoxication. 1997 J Comp Assist Tomog 21(5): 834-836 as cited in Salzman M Methanol Neurotoxicity 2006 Clin Tox 44(1): 89-90)

**Tuesday, September 17, 2013****Question:**

What is the so-called “asp” caterpillar, what is the geographic range of these animals and what are the clinical characteristics of the envenomation they produce in humans?

**Answer:**

The asp caterpillar (*Megalopyge opercularis*), which develops in adulthood into a puss moth, is a venomous caterpillar found in the Southwestern United States. When this caterpillar rubs against the skin, venomous hairs break off and embed in the skin resulting in severe pain, burning, swelling, nausea, abdominal pain, and headache. Hemorrhagic papules usually develop in conjunction with local adenopathy and swelling. (Eagleman DM. Envenomation by the asp caterpillar (*Megalopyge opercularis*) 2008 Clin Tox 46(3):201-205)

**Monday, September 16, 2013****Question:**

What is the difference, based on gender, in morning driving risk after taking the zolpidem containing products (e.g. Ambien, Ambien-CR, Edluar, and Zolpimist) for sleep?

**Answer:**

Females clear the drug zolpidem more slowly than males. Thus, at the same nighttime dose of this drug, females will be expected to demonstrate higher blood levels the next morning and presumably greater decrements in driving function and ability. (Farkas RH et al. Zolpidem and driving impairment-Identifying persons at risk. 2013 NEJM 369(8):689-691)

**Friday, September 13, 2013****Question:**

One important source for environmental hexavalent chromium has historically been associated with waste water from cooling towers. Why is this form of chromium found in cooling towers?

**Answer:**

Cooling towers often use hexavalent chromium as an anti-corrosive agent and rust inhibitor for their submerged moving parts. This situation was highlighted in the movie “Erin Brockovich” which was based on the 1987 events involving Pacific Gas and Electric (PG&E), a large utility that detected elevated concentrations of hexavalent chromium in a groundwater monitoring well near the Mojave Desert town Hinkley, California. PG&E had reportedly discharged large amounts of waste water contaminated with hexavalent chromium into unlined retention ponds and that waste water reportedly leached into the local groundwater. (Pellerin C and Booker SM. Reflections on hexavalent chromium: health hazards of an industrial heavyweight. 2000 Environ Health Perspect 108:A401-407)

**Thursday, September 12, 2013****Question:**

In July of 1985, three adults who ate a solid green watermelon purchased in Oakland, California, had rapid onset of nausea, vomiting, diarrhea, profuse sweating, excessive tearing, muscle fasciculations, and bradycardia. Subsequently other clusters of similar disease were reported in a number of western states as well as western Canada. What toxicant was involved in this well-known poisoning event?

**Answer:**

The culprit toxicant was aldicarb sulfoxide (ASO), which was detected in the melons. ASO is the primary toxic metabolite of aldicarb (Temik), a carbamate insecticide that was not registered at the time in the US for use on watermelons. (Epidemiologic notes and reports of aldicarb food poisoning from contaminated melons-California. April 25, 1986 MMWR 35(16): 254-258)

**Wednesday, September 11, 2013****Question:**

Ammonium nitrate (AN) is an industrial chemical that has been part of a number of disastrous industrial (and other) explosions over the past 50 years. “Pure” AN is considered to be stable but is capable of exploding under extraordinary circumstances. What circumstances may be expected to render AN prone to explosion?

**Answer:**

AN is known to “self compress” and “self confine” under some circumstances making it much more likely to explode. In addition, AN is at risk for explosion when stored near other material that can add fuel to the AN – such as grain, sugar, seeds, sawdust, and most especially petroleum fuels such as diesel. Finally, AN is a powerful oxidizer and a rich source of nitrate, which provides energy to an explosion. Thus, the presence of fuel and/or heat (and especially both) near AN is a very high hazard situation. (EPA, OSHA and ATF document, August, 2013, “Chemical Advisory: Safe Storage, Handling, and Management of Ammonium Nitrate”. Accessed at [http://www.epa.gov/emergencies/docs/chem/AN\\_advisory.pdf](http://www.epa.gov/emergencies/docs/chem/AN_advisory.pdf))

**Tuesday, September 10, 2013****Question:**

What is degreasers' flush?

**Answer:**

According to the National Institute of Occupational Safety and Health (NIOSH), degreasers' flush involves facial and other skin flushing and can occur in workers imbibing alcohol following industrial exposure to trichloroethylene (TCE) vapor. The dermal response of flush reaches maximum intensity 30 minutes after onset and fades within approximately 60 minutes. (<http://www.cdc.gov/niosh/topics/skin/occderm-slides/occderm18.html>)

**Monday, September 9, 2013****Question:**

What is the average ratio of serum ethanol concentration to blood ethanol concentration in humans? In other words, how does one convert serum ethanol levels into whole blood ethanol levels?

**Answer:**

The average ratio of serum ethanol to blood ethanol has been reported to be 1.15:1 (reported range of 0.88 to 1.59). Thus dividing a measured serum alcohol concentration by 1.15 results in the estimated blood ethanol concentration. (Rainey PM. Relation between serum and whole blood ethanol concentrations. 1993 Clin Chem 39:2288-2292)

**Friday, September 6, 2013**

**Question:**

The beverage absinthe has enjoyed popularity at various times over the past several hundred years despite concerns regarding the potential toxic effect of the constituent chemical thujone. How was absinthe originally manufactured?

**Answer:**

The cited reference notes "Absinthe was classically manufactured from dried wormwood (*Artemisia absinthium*), anise, and fennel, which were steeped overnight in 85% (by volume) ethanol. The next day water was added, the concoction boiled and the distillate (alcohol plus steam distilled terpenoids) collected. The process was completed by a further extraction of dried Roman wormwood, hyssop and lemon balm and filtration to yield a clear green liqueur of 74% alcohol." This clear green liqueur is absinthe. (Strang J et al. Absinthe: what's your poison? 1999 BMJ 319:1590-1592)

**Thursday, September 5, 2013**

**Question:**

What is considered to be the most consistent clinical manifestation of dioxin toxicity?

**Answer:**

Chloracne is considered to be the most consistent clinical manifestation of dioxin toxicity. (Ju Q, et al. Environmental pollution and acne: Chloracne. 2009 Dermato-Endocrinology 1(3);125-128)

**Wednesday, September 4, 2013**

**Question:**

The ingestion of seed treated with what chemical was responsible for an epidemic of porphyria cutanea tarda in Turkey during the period 1956 through 1969.

**Answer:**

The ingestion of seed treated with hexachlorobenzene was responsible for an epidemic of porphyria cutanea tarda in Turkey during the period 1956 through 1969. (Ferrer A and Cabral R. Recent epidemics of poisoning by pesticides. 1995 Tox Letters 82/83:55-63)

**Tuesday, September 3, 2013**

**Question:**

What are the clinical characteristics of the so-called "iron pill aspiration" (IPA) syndrome?

**Answer:**

Ferrous sulfate is the most common iron preparation related to the "iron pill aspiration" (IPA) syndrome which is characterized by the triad: history of aspiration of iron containing pill, intense airway inflammation, and iron particles in bronchial biopsy specimens. (Lee P et al. Syndrome of iron pill aspiration. 2002 Chest 121(4): 1355-1357 as cited in Kupeli E et al. "Pills" and the air passages. 2013 Chest 144(2):651-660)

**Monday, September 2, 2013**

**Question:**

Which form of stroke may be positively associated with short-term exposure to outdoor air pollution; hemorrhagic stroke or ischemic stroke?

**Answer:**

A recent study evaluated the effects of suspended particulate matter on cardiovascular mortality with special focus on stroke type. After adjusting for exposure to atmospheric dusts, the authors of the cited study concluded that short-term exposure to outdoor air pollution (particulate matter < 8 microns aerodynamic diameter) may increase the risk for both hemorrhagic and ischemic stroke. (Yorifuji T and Kashima S. Associations of particulate matter with stroke mortality. 2013 J Occ Env Med 55(7):768-771)

**Friday, August 30, 2013**

**Question:**

What is DPTA and exposure to what substances might warrant the use of this agent?

**Answer:**

DPTA is diethylenetriamine pentaacetate. This drug is capable of binding radioactive plutonium, americium, and curium in order to decrease the amount of time it takes to get these isotopes out of the body. DPTA is formulated at either calcium-DTPA or zinc-DTPA. When given within the first day after internal contamination has occurred, Ca-DTPA is more effective than Zn-DTPA. After 24 hours have passed, Ca-DTPA and Zn-DTPA are equally effective. (<http://emergency.cdc.gov/radiation/dtpa.asp>)

**Friday, August 30, 2013**

**Question:**

Clarification: Today's question contained multiple typographical errors. The correct compound is DTPA not DPTA. We apologize for the errors.

**Answer:**

**Thursday, August 29, 2013**

**Question:**

When threatened, certain species of cobra are able to spit their venom towards the face of the human or animal that is providing the perceived threat. How far can a spitting cobra eject venom and do cobras spit their venom in defensive situations in fixed or random patterns?

**Answer:**

If threatened, spitting cobras can eject their venom up to approximately 3 meters. The cited reference describes a study where the results indicated that the spray pattern of spitting cobras is not fixed and that the snake matches the pattern of venom distribution to the size of the target in a fashion that appears to be independent of target distance. (Berthe RA et al. Spitting cobras adjust their venom distribution to target distance. 2009 J Comp Physiol A 195:753-757)

**Wednesday, August 28, 2013**

**Question:**

What is the initial clinical presentation of pediatric aged patients following the ingestion of the mushroom *Amanita phalloides*? When would liver failure be expected to manifest following this ingestion?

**Answer:**

The cited reference notes "Initially, the patients suffer from abdominal pain, vomiting, and watery diarrhea after an asymptomatic incubation period of 6–12 h after mushroom ingestion. The hepato-renal period with signs of liver failure starts 24 to 72 hours after an interval free of complaints. Patients usually develop rapid loss of organ function with severe bleeding complications due to coagulopathy, renal insufficiency, cardiopulmonary failure, and HE. (Grabhorn E et al. Successful outcome of severe *Amanita phalloides* poisoning in children. 2013 *Pediatr Transplantation* 17:550-555)

**Tuesday, August 27, 2013**

**Question:**

Ipecac syrup was used frequently in the past by clinicians to induce vomiting in an attempt to decontaminate the upper GI tract. Where is ipecac derived from? What are the two primary components of ipecac and which of these constituents is the more cardiotoxic?

**Answer:**

The authors of the cited reference note that "ipecac is derived from dried roots and rhizomes of the *Cephaline ipecacuanha* plant; its chief pharmacologic properties are due to its alkaloid components, emetine and cephaline. Of the two alkaloids, emetine is found to be the more cardiotoxic and constitutes more than half of the alkaloid content of ipecac." (Yen M and Ewald MB. Toxicity of weight loss agents. 2012 *J Med Toxicol* 8:145-152)

**Monday, August 26, 2013**

**Question:**

Human anthrax generally occurs in one of three forms: cutaneous, pulmonary and gastrointestinal. Which of these forms accounts for the majority of all anthrax cases on a worldwide basis?

**Answer:**

Cutaneous anthrax accounts for 95% of human cases worldwide. (Doganay M et al. A review of cutaneous anthrax and its outcome. 2010 *J Infection and Pub Health* 3:98-105)

**Friday, August 23, 2013**

**Question:**

When do Mee's lines associated with thallium toxicity typically develop?

**Answer:**

Mee's lines associated with thallium toxicity typically develop between 2 and 4 weeks following exposure. (Hoffman RS. Thallium toxicity and the role of Prussian Blue in therapy. 2003 *Toxicol Rev* 22(1):29-40)

**Thursday, August 22, 2013**

**Question:**

What is *Claviceps purpurea* and what toxic syndrome results when *C. purpurea* is ingested?

**Answer:**

*Claviceps purpurea* is a fungus known to infect rye and related grains. Ingestion of the alkaloids produced by this fungus can cause painful ergotism characterized by hallucinations, mania, psychosis, seizures, and vasoconstrictive effects due to strong alpha-agonist effects and central sympatholysis. The authors of the cited reference note "Limb ischemia with paresis, impairment of sensation and ultimately loss of the affected extremity may result". They also point out that "In the Middle Ages, painful ergotism (characterized by a sensation of burning) was known as "Holy Fire" or "St. Anthony's fire," named for the monks of the Order of St. Anthony who cared for affected patients." (Frohlich G et al. Holy fire in an HIV positive man: a case of 21st-century ergotism. 2010 *CMAJ* 182(4): 378-380)

**Wednesday, August 21, 2013**

**Question:**

Vacor was a rat poison commonly used and marketed in the US from 1975 through 1979. What is the chemical name for Vacor rat poison and what is the primary pathological lesion resulting from the ingestion of this particular rat poison compound?

**Answer:**

Vacor rat poison contained the chemical n-3-pyridyl-methyl-n-P-nitrophenyl-urea (PNU). Following ingestion, this chemical was reported to cause irreversible diabetes mellitus resulting from complete destruction of pancreatic beta islet cells. PNU also was associated with the development of autonomic and peripheral neuropathies. (Peters KS et al. Diabetes mellitus and orthostatic hypotension resulting from ingestion of Vacor rat poison: Endocrine and autonomic function studies. 1981 *West J Med* 134(1): 65-65)

**Tuesday, August 20, 2013**

**Question:**

Some workers in the semiconductor industry and in some aspects of ore refining industries may be at risk for exposure to arsine. What are the physical characteristics of arsine and what are the clinical characteristics, including the most common complications, associated with clinically significant exposure to arsine.

**Answer:**

Arsine is a gas that is colorless and non-irritating. It is approximately 2 ½ times more dense than air. It is soluble in water and usually manifests a “fishy” or “garlicky” odor at concentrations in excess of 0.5 ppm. Following acute exposure patients may manifest dizziness, malaise, nausea, abdominal pain and difficulty breathing. These symptoms are usually slightly delayed following exposure but usually appear within a few hours of exposure. The most serious complications of arsine gas exposure include massive hemolysis with consequent hypoxia and renal failure. (Pullen-James and Woods SEW. Occupational arsine gas exposure. 2006 J National Med Assoc. 98(12): 1998-2001)

**Monday, August 19, 2013****Question:**

The FDA recently approved the drug Diclegis for nausea and vomiting of pregnancy. This drug is a fixed dose, delayed release combination of doxylamine and the vitamin B6 analog pyridoxine. Doxylamine and pyridoxine were previously available in what drug that was voluntarily withdrawn from the US market in 1983 due to claims of teratogenicity that were eventually disproven?

**Answer:**

Doxylamine and pyridoxine were previously available in a fixed dose combination known as Bendectin. Bendectin was removed from the market in 1983 but the claims of teratogenicity associated with this drug were eventually disproven. (The Medical Letter. August 5, 2013, 55(1422):61-62)

**Friday, August 16, 2013****Question:**

Thalidomide is sometimes used in the treatment of certain refractory dermatologic and oncologic diseases (e.g. graft-vs-host (GVH) disease, pyoderma gangrenosum and discoid lupus). While thalidomide has been associated with a well-described embryopathy, in other cases, the development of a toxic neuropathy may limit the use of this drug. What characterizes thalidomide-induced neuropathy?

**Answer:**

Thalidomide induces a dose-dependent sensorimotor, length-dependent, axonal neuropathy. The authors of the cited reference caution that thalidomide “should be judiciously used with close neurologic monitoring”. (Chaudhry V. et al. Thalidomide-induced neuropathy. 2002 Neurology 59:1872-1875)

**Thursday, August 15, 2013****Question:**

Various formulations of prenatal, pediatric and adult vitamin products as well as single ingredient iron tablets are available and contain iron salts with varying amounts of iron. What is the percentage of elemental iron contained in the iron salts ferrous fumarate, ferrous sulfate and ferrous gluconate?

**Answer:**

Ferrous fumarate contains 33% elemental iron, ferrous sulfate contains 20% elemental iron and ferrous gluconate contains 12 % elemental iron. (Manoguerra AS et al. Iron ingestion: An evidence based consensus guideline for out-of-hospital management. 2005 Clin Tox 43: 553-570)

**Wednesday, August 14, 2013****Question:**

Lithium toxicity is usually associated with neurologic symptoms. However, in some cases, manifestations of cardiac toxicity may occur. What are the documented cardiac manifestations associated with lithium toxicity?

**Answer:**

The documented cardiac effects associated with lithium toxicity include nonspecific T wave changes, ST segment changes, QTc prolongation, sinus node dysfunction, AV blocks, and ventricular dysrhythmias. (Offerman SR et al. Hospitalized lithium overdose cases reported to the California Poison Control System 2010 Clin Tox 48(5): 443-448)

**Tuesday, August 13, 2013****Question:**

What is believed to be the mechanism for renal injury related to the ingestion of mercuric chloride?

**Answer:**

Patients who ingest mercuric chloride may develop oliguria and renal failure. The mechanism for this is thought to involve decreased renal blood flow in combination with direct toxicity to kidney tissue. The typical renal pathology associated with mercuric chloride ingestion involves injury to the proximal tubules. The cited reference notes “Tubular impairments and necrosis are more common than glomerular effects.” (Beasley DMG, et al. Full recovery from a potentially lethal dose of mercuric chloride. 2013 J Med Tox. Published online 13 June 2013)

**Monday, August 12, 2013****Question:**

Brodifacoum is a common active ingredient in commercially available rodenticides in the US and when present is traditionally found in a 0.005% concentration. What is the presumed half-life of brodifacoum after overdose? What is its duration of action following overdose?

**Answer:**

The half-life of brodifacoum ranges from 16 to 34 days after overdose and the duration of action ranges from 51 days to 9 months following overdose. (Caravati EM, et al. Long acting anticoagulant rodenticide poisoning: An evidence based consensus guideline for out-of-hospital management. 2007 Clin Tox 45(1):1-22)

**Friday, August 9, 2013****Question:**

Which serotonin reuptake inhibitor (SSRI) does not significantly prolong the QT interval and also has the fewest drug interactions?



**Answer:**

Sertraline (Zoloft and generics) is the SSRI that does not significantly prolong the QT interval and also exhibits the fewest drug interactions. (The Medical Letter, July 22, 2013, 55(1421): 59)

**Thursday, August 8, 2013****Question:**

What toxin is found in pufferfish? Which organs in the pufferfish have the highest concentration of this toxin?

**Answer:**

The pufferfish toxin is tetrodotoxin, a potent neurotoxin. In most species, the liver and ovary have the highest toxicity, followed by intestines and skin. (Noguchi T and Arakawa O. Tetrodotoxin- distribution and accumulation in aquatic organisms, and cases of human intoxication. 2008 Marine Drugs 6:220-242)

**Wednesday, August 7, 2013****Question:**

Which of the following contains the highest concentration of methyl salicylate: Tiger oil, Red Flower oil, Oil of Wintergreen or Ben-Gay Extra Strength Cream?

**Answer:**

Oil of Wintergreen contains the highest percentage of methyl salicylate (98%). The other listed products contain methyl salicylate as noted Tiger Oil (38%); Red Flower Oil (67%); Ben-Gay Extra Strength Cream (30%). (Davis JE. Are one or two dangerous? Methyl salicylate exposure in toddlers. 2007 32(1): 63-69)

**Tuesday, August 6, 2013****Question:**

The so-called "pallidus index" (PI) addresses an MRI finding referable to exposure to what toxicant? What exactly is the "pallidus index"?

**Answer:**

The "pallidus index" refers to an attempt to quantify the accumulation of manganese within the globus pallidus of the brain. The pallidus index is "the ratio of the signal intensity in the globus pallidus to that in the subcortical frontal white matter in axial T1-weighted MRI planes multiplied by 100". This term represents a semi-quantitative indicator of brain manganese status and has been applied in a variety of human studies. (Krieger D et al. Manganese and chronic hepatic encephalopathy. 1995 Lancet 346:279-84 as cited in Zheng W et al. Biomarkers of manganese intoxication 2011 Neurotoxicology 32:1-8)

**Monday, August 5, 2013****Question:**

What percentage of individuals who receive dimercaprol (BAL) for the treatment of lead poisoning will experience side effects?

**Answer:**

According to the Centers for Disease Control and Prevention, "between 30% and 50% of patients who receive BAL will experience side effects. Mild febrile reactions and transient elevations of hepatic transaminases may be observed. Other minor adverse effects include, in order of frequency, nausea and occasional vomiting, headache, mild conjunctivitis, lacrimation, rhinorrhea, and salivation. Most side effects are transient and rapidly subside as the drug is metabolized and excreted. Intravenous hydration coupled with restricting oral intake can circumvent, in large part, gastrointestinal distress. BAL should not be used for children (or adults) who are allergic to peanuts or peanut products as this drug is formulated as a suspension in peanut oil. (<http://www.cdc.gov/nceh/lead/publications/books/plpyc/appendix2.htm#BAL>)

**Friday, August 2, 2013****Question:**

What is the concept of hormesis?

**Answer:**

According to the cited reference, "Hormesis is a dose-response relationship characterized by a low dose stimulation and a high dose inhibition. The hermetic dose response has been typically represented in graphs as an inverted U- or J-shaped dose response, depending on the endpoint measured." (Calabrese EJ. Getting the dose-response wrong: why hormesis became marginalized and the threshold model accepted? 2009 Arch Toxicol 83:227-247)

**Thursday, August 1, 2013****Question:**

Based on Drug Enforcement Agency (DEA) reported data regarding clandestine methamphetamine labs, which state had the highest number of total clandestine meth lab incidents including the discovery of labs, meth lab dumpsites, or the finding of meth lab related chemicals and/or lab equipment from the operation of a meth lab?

**Answer:**

Based on DEA reported data, in the year 2012, Missouri had the highest number of clandestine meth lab incidents (n=1825) as defined above. (<http://www.justice.gov/dea/resource-center/meth-lab-maps.shtml>. Accessed July 2013)

**Wednesday, July 31, 2013****Question:**

The yew (*Taxus baccata*) is a conifer that is commonly found. Which toxins are contained in this plant and what specific plant parts contain these toxins? Finally, what is the mechanism for toxicity produced by the toxin found in this plant?

**Answer:**

The most important toxins contained in *Taxus baccata* are taxine A and taxine B. All green or dry parts of the tree, except for the berry or aril, contain taxines. These taxines are toxic alkaloids and are blockers of cardiac sodium and calcium channels. (Panzer C. et al. Extracorporeal life support in a severe *Taxus baccata* poisoning. 2010 Clin Tox 48 (5):463-465)

**Tuesday, July 30, 2013**

**Question:**

What toxin has been identified as an important factor in the pathogenesis of the enteric pathogen *Campylobacter jejuni*?

**Answer:**

The most important virulence factor within the genome of *C. jejuni* is the so-called cytolethal distending toxin (CDT). The precise role of CDT in diarrheal disease caused by *C. jejuni* is not yet elucidated but it is likely this toxin arrests the G2 phase of the cell cycle. The authors of the cited reference note that CDT induced cell cycle arrest within intestinal epithelial cells presumably serves to "increase the contact time between host and pathogen" and may also serve to produce some degree of immunosuppression. (Poly F and Guerry P. Pathogenesis of *Campylobacter*. 2008 Curr Opin in Gastroenterology 24:27-31 and Lara-Tejer M and Galan JE. Cytolethal distending toxin: limited damage as a strategy to modulate cellular functions. 2002 Trends Microbiol 10:147-152)

**Monday, July 29, 2013**

**Question:**

What are the absorption, distribution, and elimination characteristics of the drug colchicine?

**Answer:**

Colchicine is rapidly absorbed with serum levels peaking at 0.5-3.0 hours post ingestion and is rapidly distributed to all tissues. Its protein binding is 10-50% in therapeutic doses and the volume of distribution ranges from 2 and 12 L/Kg but may be as high as 21 L/Kg in overdose. It undergoes extensive hepatic first pass metabolism and elimination is primarily via hepatic metabolism by cytochrome P450 (CYP 3A4) mediating deacetylation and demethylation followed by biliary excretion. The mean elimination half-time of oral colchicine is 4.4-16 hours in therapeutic doses but may be as high as 11-32 hours in the overdose setting. (Finkelstein Y et al. Colchicine poisoning: the dark side of an ancient drug. 2010 Clin Tox 48(5): 407-414)

**Friday, July 26, 2013**

**Question:**

What is the primary toxin in the mushroom *Gyromitra esculenta*?

**Answer:**

The primary toxin in the mushroom *Gyromitra esculenta* is gyromitrin. This chemical is easily hydrolyzed by either gastric acid or by cooking into methylformylhydrazine and is ultimately converted into the chemical monomethylhydrazine (MMH). The authors for the cited reference note that MMH may "cause gastrointestinal irritation, hemolysis and methemoglobin formation". (Leatham A and Dorran TJ. Poisoning due to raw *Gyromitra esculenta* (false morels) west of the Rockies. 2007 J Canadian Assoc Emerg Physicians 9(2):127-130)

**Thursday, July 25, 2013**

**Question:**

What are the EKG effects associated with methylphenidate overdose?

**Answer:**

One recent study looking at 23 cases of methylphenidate overdose reported no cardiac arrhythmias and a normal mean heart rate (approximately 92 beats per minute). In addition, these authors concluded that methylphenidate overdose is "unlikely to have substantial effects on the QRS or QT intervals". (Hill SI, et al. Electrocardiographic effects of methylphenidate overdose. 2010 Clin Tox 48(4): 342-346)

**Wednesday, July 24, 2013**

**Question:**

Describe the venom delivery system in the Gila monster (*Heloderma suspectum*). What is the character of the venom produced by the Gila monster? What are the clinical characteristics of envenomation by the Gila monster?

**Answer:**

The venom delivery system is made up of paired glands on both sides of the lower jaw of this lizard. Venom is transported via ducts to the base of grooved teeth along the mandible. It is through these grooved teeth and via repeated chewing motion that the venom is delivered into the bite wound. Gila monster venom contains a variety of potentially harmful proteins including hyaluronidase, phospholipase A, gilatoxins, and kallikrein-like toxins. The clinical characteristics of envenoming by the Gila monster include substantial local pain and swelling along with weakness and nausea. Vomiting, diaphoresis, hypotension and tachycardia have also been reported. Some reported cases have involved severe anaphylaxis and airway edema. (French RN, et al. Gila monster bite. 2012 Clin Tox 50(2):151-152)

**Tuesday, July 23, 2013**

**Question:**

Electrophysiological studies may be helpful in confirming the clinical diagnosis of food-borne botulism. What specific electrophysiological findings are diagnostic of food-borne botulism and also exclude similar neurological problems including the Miller Fischer variant and Guillain-Barre syndrome?

**Answer:**

The findings of CMAP (compound muscle action potential) with post-exercise facilitation are diagnostic of botulism and excludes similar neurological problems including the Miller Fischer variant and Guillain-Barre syndrome. (Witoonpanich R et al. Survival analysis for respiratory failure in patients with food borne botulism. 2010 Clin Tox 48(3):177-183)

**Monday, July 22, 2013**

**Question:**

Carotenemia in infancy is an uncommon condition characterized by an abnormal yellowish orange pigmentation of the skin, most prominently seen on the palms, soles, and naso-labial folds. What is the most common etiology for this condition in infants?

**Answer:**

Carotenemia in infancy is a relatively rare but benign condition, invariably of dietary origin, that can, in some cases, be confused with jaundice. The cited reference notes “Carotenoids are organic compounds found in fruit and vegetables and include a- and b-carotene, lycopene, b-cryptoxanthin, lutein, and zeaxanthine.” The authors point out that fruits such as mangoes, apricots, and melons as well as carrots, peppers, and other green leafy vegetables contain these compounds in abundance. They go on to describe that “Homogenization and pureeing of foods (as is commonly done for infant feedings) increase the bioavailability of these carotenoids. Carotenoids accumulate in the epidermis about 2 weeks after serum levels achieve equilibrium, and maximum accumulation occurs in areas with large numbers of sweat glands including the naso-labial folds, palm, and soles.” (Karthik S., et al. Carotenemia in infancy and its association with prevalent feeding practices. 2006 *Pediatr Derm* 23(6): 571–573)

**Friday, July 19, 2013****Question:**

What is the association between ambient environmental temperatures and adverse clinical outcomes following cocaine overdose?

**Answer:**

In a landmark study, the first cited reference listed below reported that 25% of all individuals younger than 55 years who died from hyperthermia in New York City had used cocaine immediately prior to their deaths. These authors also reported that the mean number of deaths from cocaine overdoses on days in which the temperature was equal to or greater than 88 degrees F was 33% higher than the mean on days with lower maximum temperature. According to these authors, “The reported association of ambient temperature with drug overdose mortality appears specific to cocaine...” (Marzuk PM et al. Ambient temperature and mortality from unintentional cocaine overdose. 1998 *JAMA* 279(22): 1795-1800) These findings have been more recently verified by authors who report “a significant relation between temperature and accidental overdose fatality for all models where the overdoses were due in whole or in part to cocaine but not for non-cocaine overdoses”. (Bohnert AS et al. Ambient temperature and risk of death from accidental drug overdose in New York City 1990-2006. 2010 *Addiction* 105(6):1049-1054)

**Thursday, July 18, 2013****Question:**

What is the “pica habit” and how does pica in pregnant females result in the potential for elevated blood lead levels?

**Answer:**

According to the cited reference, pica is “the craving for and intentional ingestion of substances not defined as food”. The authors go on to describe that “Pica has been reported in the US as a common practice among pregnant women with one review of 13 studies published from 1950 to 1987 documenting pica prevalence ranging from 10 to over 60%. Three of the most frequently ingested nonfood substances are earth (clay, crushed pottery, and soil), starches (cornstarch, uncooked rice, and flour), and ice. Since these nonfoods, particularly earth, can be lead-contaminated, ingesting them increases the risk for lead poisoning.” (Thihalolipavan S et al. Examining pica in NYC pregnant women with elevated blood lead levels. 2013 *Matern Child Health J* 17(1):49-55)

**Wednesday, July 17, 2013****Question:**

Which groups of individuals are at increased risk for the development of latex allergy?

**Answer:**

Specific occupations including healthcare workers, dentists, rubber plantation workers, food handlers, security personnel, greenhouse workers, construction workers, hairdressers, domestic workers, individuals who have undergone multiple surgical procedures, patients with spina bifida (frequent self catheterizers), patients with atopy and eczema as well as those with allergies to certain foods (banana, avocado, chestnut, kiwi, papaya, mango, bell pepper, fig, tomato, celery and potato) have been noted to be at increased risk for latex allergy. In addition individuals with the IL-13 and IL-18 promoter polymorphisms may be at increased risk. (Rolland JM and O’Hehir RE. Latex allergy: a model for therapy. 2008 *Clin and Experimental Allergy*, 38, 898–912)

**Tuesday, July 16, 2013****Question:**

What is the only reported case of human poisoning by ricin administered via the intramuscular route and what was the resulting histopathology reported in that case?

**Answer:**

The only reported case of human poisoning by ricin administered via the intramuscular route involved Bulgarian dissident writer Georgi Markov who was murdered by ricin injection in 1978. The author of the cited work noted: “From the pellet which was introduced into his thigh muscle, ricin was distributed around his body, and many tissues were affected. Damage included the presence of severe local lymphoid necrosis (in the inguinal lymph nodes which drained the injection site), liver necrosis, diffuse inflammation of the kidneys and spleen. Hemorrhagic necrosis of the small intestine was also noted as well as the pancreas and testes. The myocardium and conducting tissues were found to have petechial hemorrhages which also featured in adrenals, gut wall and lymph nodes. A mild pulmonary edema observed was thought to have been secondary to cardiac failure. The key feature of toxicity via the intramuscular/intravascular route is the fairly rapid distribution of toxin around the body to most organs, making therapeutic treatment a challenge.” (Griffiths GD. Understanding ricin from a defensive viewpoint. 2011 *Toxins* 3:1373-1392 and Crompton R. Georgi Markov- Death in a pellet 1980 *Med Leg J* 48:51-62)

**Monday, July 15, 2013****Question:**

The available antimalarial drugs in use today are associated with a wide variety of potential adverse effects. Which antimalarial is associated with vomiting, headache, insomnia, vivid dreams, anxiety, dizziness and the development of psychosis?

**Answer:**

Mefloquine has been associated with vomiting, headache, insomnia, vivid dreams, anxiety, dizziness and the development of psychosis? (Baird JK. Effectiveness of antimalarial drugs. 2005 *NEJM* 352:1565-1577)

**Friday, July 12, 2013****Question:**

What are the clinical symptoms associated with shigellosis? What are the pathogenic mechanisms associated with Shigella related disease?

**Answer:**

Shigellosis is commonly associated with fever, bright-red bloody diarrhea, and crampy abdominal pain. The cited reference notes “Shigella is similar to salmonella in that it possesses a large plasmid that encodes the principal T3SS and other virulence factors for invasion.”

The authors go on to note “the pathogenic mechanism of shigellosis is complex, involving Shiga toxins (enterotoxin, cytotoxin, and neurotoxin), cytokine-mediated inflammation of the colon, and necrosis of the colonic epithelium. The resulting colitis and ulceration of the mucosa results in bloody (bright red) mucoid stools, febrile diarrhea, or both. (Ross A., et al. Enteropathogens and chronic illness in returning travelers. 2013 NEJM 368: 1817-1825)

**Thursday, July 11, 2013****Question:**

Which plant is a member of the Solanaceae group and has roots, leaves and fruits containing atropine, hyoscyamine, and scopolamine?

**Answer:**

Deadly nightshade (*Atropa belladonna*) is a member of the Solanaceae group and has roots, leaves and fruits containing atropine, hyoscyamine, and scopolamine. (Caksen H et al. Deadly nightshade (*Atropa belladonna*) intoxication: an analysis of 49 children. 2003 Human & Experimental Toxicology 22: 665-668)

**Wednesday, July 10, 2013****Question:**

When does the FDA recommend the use of a “boxed warning” to be included in prescribing information for any given drug?

**Answer:**

A boxed warning is ordinarily used to highlight for prescribers one of the following situations:

1-There is an adverse reaction so serious in proportion to the potential benefit from the drug (e.g., a fatal, life-threatening or permanently disabling adverse reaction) that it is essential that it be considered in assessing the risks and benefits of using the drug ?OR

2-There is a serious adverse reaction that can be prevented or reduced in frequency or severity by appropriate use of the drug (e.g., patient selection, careful monitoring, avoiding certain concomitant therapy, addition of another drug or managing patients in a specific manner, avoiding use in a specific clinical situation) ?OR

3-FDA approved the drug with restrictions to ensure safe use because FDA concluded that the drug can be safely used only if distribution or use is restricted (Guidance for Industry Warnings and Precautions, Contraindications, and Boxed Warning Sections of Labeling for Human Prescription Drug and Biological Products—Content and Format. U.S. Department of Health and Human Services Food and Drug Administration?Center for Drug Evaluation and Research (CDER) Center for Biologics Evaluation and Research (CBER) October 2011. Accessed at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075096.pdf>)

**Tuesday, July 9, 2013****Question:**

What is the association of the p53 gene with cigarette smoke-related lung cancers in humans?

**Answer:**

The p53 gene is an important tumor suppressor gene and is frequently mutated in a variety of human cancers. For example mutation of this gene occurs in a majority (> 50%) of aflatoxin B1-associated liver cancers. With regard to cigarette smoke (CS)-related lung cancers, the cited reference reports “The p53 gene is the most frequently mutated tumor suppressor gene in CS-related lung cancers, and its mutational pattern is distinctly different from that found in lung cancers of nonsmokers.” (Feng Z et al. Acrolein is a major cigarette-related lung cancer agent: preferential binding at p53 mutational hotspots and inhibition of DNA repair. 2006 PNAS 103(42): 15404-15409)

**Monday, July 8, 2013****Question:**

In what industrial applications are the chemicals gallium arsenide (GaAs), indium arsenide (InAs) and aluminum gallium arsenide (AlGaAs) found?

**Answer:**

The chemicals gallium arsenide (GaAs), indium arsenide (InAs) and aluminum gallium arsenide (AlGaAs) are found in semiconductor applications, solar cells, light emitting diodes, lasers and integrated circuits. (Tanaka A. Toxicity of indium arsenide, gallium arsenide and aluminum gallium arsenide. 2004 Tox Appl Pharm 198:405-411)

**Friday, July 5, 2013****Question:**

What is an irritant chemical?

**Answer:**

The cited reference notes that an irritant is “a noncorrosive chemical that causes a reversible chemical inflammatory reaction on direct contact with the skin, eyes, nose or respiratory system. The actions of an irritant are nonspecific and do not entail an immunologic mechanism. Mechanistically, the effects may stem from an irritant’s facility to react with different chemicals, such as sulfur or cysteine molecules, or form double bonds with human proteins.” (Brooks SM and Bernstein IL. Irritant-induced airway disorders. 2011 Immunol Allergy Clin N Am 31:747-768)

**Thursday, July 4, 2013****Question:**

What are the clinical features of diethylene glycol (DEG) poisoning?

**Answer:**

According to the cited reference, the clinical features of DEG poisoning involve three stages: “The first phase consists of gastrointestinal symptoms with evidence of inebriation and developing metabolic acidosis. If poisoning is pronounced, patients can progress to a second phase with more severe metabolic acidosis and evidence of emerging renal injury, which, in the absence of appropriate supportive care, can lead to death. If patients are stabilized, they may then enter the final phase with various delayed neuropathies and other neurological effects, sometimes fatal.” (Shep LJ et al. Diethylene glycol poisoning. 2009 Clin Tox 47(6):525-535)

**Wednesday, July 3, 2013**

**Question:**

What is the relationship between smoking-caused lung cancer and radon exposure related lung cancer?

**Answer:**

There is a strong synergy between smoking as a cause for lung cancer and radon as a cause for lung cancer. The cited reference points out that "...the absolute magnitude of the lung cancer risk associated with radon exposure is significantly higher for ever-smokers than for never-smokers. It is estimated that 86% of radon-related lung cancer deaths are in current and former smokers". (Lantz PM et al. Radon, smoking and lung cancer: The need to refocus radon control policy. 2013 Am J Pub Health 103:443-447)

**Tuesday, July 2, 2013**

**Question:**

What was the so-called "Seveso disaster"?

**Answer:**

The Seveso, Italy, disaster resulted in TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) exposure to a wide population in and around Seveso, Italy, on July 10, 1976. This environmental disaster took place in the trichlorophenol production department of a chemical plant located near the town of Seveso, approximately 25 km north of Milan, when a chemical cloud containing several kilograms of TCDD was released into the atmosphere. (Consonni D., et al. Mortality in a population exposed to dioxin after the Seveso, Italy, accident in 1976: 25 years of follow up. (2008 Am J Epidemiology 167(7): 847-858)

**Monday, July 1, 2013**

**Question:**

What is the most common cause for human illness due to fish poisoning in the US?

**Answer:**

Scombroid is the most common cause for human illness due to fish poisoning in the US. The cited reference notes "Between 1998 and 2002, there were 118 outbreaks of confirmed scombroid fish poisoning affecting 463 people with no deaths reported. In 2006, there were 30 outbreaks with 102 cases with no deaths reported." (Codori N and Marinopoulos S. Scombroid fish poisoning after eating seared tuna. 2010 So Med J 103(4): 382-384)

**Friday, June 28, 2013**

**Question:**

Which medications are currently approved by the FDA for the treatment of alcohol dependence?

**Answer:**

The FDA approved medications for the treatment of alcohol dependence are disulfiram, acamprosate, and two forms of naltrexone (oral and extended-release injectable). The cited reference notes that "All are modestly effective but greatly underused". (Friedmann PD. Alcohol use in adults. 2013 NEJM 368(4):365-373)

**Thursday, June 27, 2013**

**Question:**

Severe salicylate intoxication is frequently associated with metabolic acidosis and a co-existing respiratory alkalosis. What is the nature of this respiratory alkalosis?

**Answer:**

The respiratory alkalosis associated with severe salicylate intoxication is not a simple compensatory response to the developing metabolic acidosis. Rather, this phenomenon represents a primary central nervous system effect of salicylate in the central nervous tissue. (Greenberg MI and Hendrickson RG. Deleterious effects of endotracheal intubation in salicylate poisoning. 2003 Ann Emerg Med 41(4))

**Wednesday, June 26, 2013**

**Question:**

Why are cyanide compounds sometimes referred to as "blood agents"?

**Answer:**

Cyanides are sometimes called "blood agents," an antiquated term still used by some in the military. At the time of the introduction of cyanide in WWI, the other chemical agents in use caused mainly local effects. In contrast, inhaled cyanide produces systemic effects and was thought to be carried in the blood, hence, the term "blood agent." (Medical Management of Chemical Casualties Handbook. US Army Medical Research Institute of Chemical Defense (USAMRICD), Fourth Edition, February 2007)

**Tuesday, June 25, 2013**

**Question:**

The chemical 1-bromopropane has seen increased industrial use over the past several years. What is 1-bromopropane and what is the basis for this increase in usage?

**Answer:**

The cited reference notes that 1-bromopropane is a volatile organobromine compound that has been "introduced recently into the industrial workplace as an alternative to chlorofluorocarbons and hydrochlorofluorocarbons, the use of which has been banned owing to their effects in depleting the ozone layer and contribution to global warming". (Samukawa M et al. A Case of severe neurotoxicity associated with exposure to 1-bromopropane, an alternative to ozone-depleting or global-warming solvents. 2012 Arch Intern Med 172(16):1257-1260)

**Monday, June 24, 2013**

**Question:**

What is M8 detection paper?

**Answer:**

M8 detection paper is used primarily by the military (and some first responder units) to detect liquid 'V', 'G' and 'H' agents. This paper contains two dyes and an acid-base (pH) indicator which changes to yellow when in contact with 'G' agents, green when in contact with liquid VX and red when in contact with liquid HD. The color change usually manifests within 30 seconds of exposure. Chemical detection papers, including the M8 paper, lacks specificity and may produce false positives. (Sferopoulos R. A review of chemical warfare agent (CWA) detector technologies and commercial-off-the shelf items. March 2009 Human Protection and Performance Division, Defense Science and Technology Organization, Australian Government Department of Defense. Accessed at: <http://www.dtic.mil/cgi-bin/GetTRDoc?AD=ADA502856>)

**Friday, June 21, 2013**

**Question:**

What is the association between exposure to general anesthesia and the development of subsequent long-term cognitive changes, including dementia in persons older than 45 years of age?

**Answer:**

The cited reference reports the analysis of 877 cases of dementia and concludes that there is no significant association between exposure to general anesthesia after age 45 and incident dementia. (Sprung J et al. Anesthesia and incident dementia: A population based, nested case-control study. 2013 Mayo Clin Proc 88(6):552-561)

**Thursday, June 20, 2013**

**Question:**

Ayurveda is a traditional medical system used by a majority of India's 1.1 billion population as well as other populations around the world. These medications have been noted to contain heavy metals and they are often available for purchase via the internet. What percentage of US-manufactured and Indian-manufactured Ayurvedic medicines purchased via the Internet contain detectable lead, mercury, or arsenic?

**Answer:**

One study reported that one-fifth of both US-manufactured and Indian-manufactured Ayurvedic medicines purchased via the Internet contain detectable lead, mercury, or arsenic. (Saper RB et al. Lead, mercury and arsenic in US and Indian manufactured Ayurvedic medicines sold via the internet. 2008 JAMA 300(8):915-923)

**Wednesday, June 19, 2013**

**Question:**

What are the clinical findings seen in methotrexate embryopathy?

**Answer:**

Case reports of methotrexate exposure during pregnancy have described a methotrexate embryopathy that includes the following characteristics as listed in the cited reference: "growth deficiency, microcephaly, hypoplasia of skull bones, wide fontanels, coronal or lambdoidal craniosynostosis, upswept frontal scalp hair, broad nasal bridge, shallow supraorbital ridges, prominent eyes, low-set ears, maxillary hypoplasia, epicanthal folds, short limbs, talipes, hypodactyly, and syndactyly." This syndrome is typically associated with exposures occurring 6 and 8 weeks post conception and at dose levels equal to or greater than 10 mg/week. (Hyoun SC et al. Teratogen update: Methotrexate, 2012 Birth Defects Res (Part A) 94:187-207)

**Tuesday, June 18, 2013**

**Question:**

'Poppers' refers to a variety of volatile alkyl nitrites often distributed in small glass vials that generate a "popping" sound when the vials are crushed. These drugs are often abused recreationally and act to relax smooth muscles in blood vessels as well as in the anal and vaginal sphincters. The use of these substances has been associated with what has come to be called "poppers dermatitis". What is "poppers dermatitis"?

**Answer:**

"Poppers dermatitis" may be the result of direct contact dermatitis or allergic type dermatitis. The cited reference points out "Direct skin contact causes irritant dermatitis, which usually resolves without scarring. As the volatile alkyl nitrite vapours are inhaled, irritant dermatitis caused by 'poppers' is mostly reported in the face or upper thoracic region. Reports on 'poppers'-induced irritant dermatitis in other areas of the skin are rare." (Schauber J and Herzinger T. 'Poppers dermatitis' 2012 Clinical and Experimental Dermatology, 37, 587-588)

**Monday, June 17, 2013**

**Question:**

Dimethyl fumarate has recently been approved for use in the treatment of relapsing forms of multiple sclerosis. The mechanism of action for this drug is not known with certainty however it's primary clinical effects may be due to activation of an important antioxidant response pathway. What are the most common adverse effects associated with dimethyl fumarate?

**Answer:**

The most common adverse effects associated with dimethyl fumarate are flushing, abdominal pain, nausea and diarrhea. The cited reference notes that potentially serious lymphopenia can occur and mean lymphocyte counts decrease by approximately 30% during the first year of treatment with this drug. (The Medical Letter June 10, 2013, 55(1418): 45-47)

**Friday, June 14, 2013**

**Question:**

What is the mechanism for the production of melanosis coli (a darkening of the colonic wall often first identified when patients undergo colonoscopy)?

**Answer:**

Melanosis coli may result from the ingestion of cascara-containing foods such as rhubarb. As the cited reference notes, "The active ingredient in these substances is anthraquinone, which causes injury to the colonic epithelial cells, resulting in the production of lipofuscin, the dark pigment seen in melanosis coli. The condition is benign and reversible. Disappearance of the pigment generally occurs within a year after a patient stops taking anthraquinone." (Kew ST and Chakravarthi S. Melanosis coli 2013 NEJM 368:2303)

**Thursday, June 13, 2013**

**Question:**

The FDA has recently warned against the use of valproate (and related compounds) specifically for migraine prevention in pregnant females. What specific adverse outcome is addressed by this warning?

**Answer:**

The cited reference notes that taking valproate (or related compounds) during pregnancy can decrease the IQ of exposed children. Recent reports have noted that at 3 years of age, 4.5 years of age, and 6 years of age IQ may be 6-11 points lower in the offspring exposed to valproate during pregnancy than those exposed to carbamazepine, lamotrigine or phenytoin. (The Medical Letter, June 10,2013, 55(1418):45)

**Wednesday, June 12, 2013****Question:**

High dose methotrexate (HDMTX) with leucovorin rescue is often used in the treatment of osteosarcoma, acute lymphoblastic leukemia (ALL), and primary central nervous system (PCNS) lymphomas. In some cases HDMTX can be associated with serious complications including hepatotoxicity, nephrotoxicity, neurotoxicity, dermatologic toxicity, mucositis, pneumonitis, and bone marrow suppression. What is the mechanism of the development of HDMTX associated nephrotoxicity and what recently introduced drug is effective in lowering serum MTX levels?

**Answer:**

HDMTX can cause nephrotoxicity by a transient decline of glomerular filtration rate as well as the intra-tubular precipitation of MTX and its metabolites in acidic urine. The recombinant enzyme carboxy-peptidase G2 (CPDG2, glucaridase) can reduce elevated serum MTX levels by the rapid hydrolysis of MTX to the inactive metabolite 2,4-diamino-N10-methyl ptericoic acid (DAMPA). (Tuffaha HW and Omar S. Glucaridase rescue in a patient with high-dose methotrexate-induced nephrotoxicity. 2011 J Oncol Pharm Prac 17:136-140)

**Tuesday, June 11, 2013****Question:**

What effects on the ability to safely operate a motor vehicle do short acting benzodiazepines (e.g. alprazolam, oxazepam, tempazepam) have at therapeutic doses?

**Answer:**

The use of short-acting benzodiazepines, at therapeutic doses, have demonstrated decrements in performance in a variety of psychomotor (e.g. simple and complex reaction time, tracking ability, etc.) as well as field sobriety (e.g. 'walk and turn' and 'one leg stand') tests. (Leung SY. Benzodiazepines, opioids and driving: An overview of the experimental research. 2011 Drug and Alcohol Review 30:281-286)

**Monday, June 10, 2013****Question:**

What is the immunopathogenesis of bee venom related systemic allergic reactions?

**Answer:**

The primary clinical findings associated with bee sting reactions (urticaria, angioedema, bronchial asthma and anaphylactic shock) are consistent with IgE-mediated type I allergy. According to the cited reference, "Immediate type skin tests with bee venom are positive in more than 95% of patients and specific IgE-antibodies to bee venom allergens can be detected in more than 90% of them during the first year after an allergic sting reaction." (Muller UR. Bee venom allergy in beekeepers and their family members. 2005 Curr Opin Allergy Clin Immunol 5:343-347)

**Friday, June 7, 2013****Question:**

"Pyramiding", "stacking" and "plateauing" are "street" terms referring to various patterns of use for androgenic anabolic steroids (AAS) by athletes. What do the terms "pyramiding", "stacking" and "plateauing" refer to?

**Answer:**

According to the cited reference, "pyramiding" is a regimen whereby the user "starts with low doses at the beginning of a cycle and then steadily increase the dose until a gradual tapering phase at the end of a cycle." "Stacking" refers to the simultaneous use of more than one AAS. "Plateauing" refers to the use of several AAS drugs in "overlapping patterns to avoid the development of tolerance". (Barceloux DG and Palmer RB. Anabolic-androgenic steroids. 2013 Disease-a-Month 59(6): 221-248)

**Thursday, June 6, 2013****Question:**

What is the WISER information system and what entity developed WISER?

**Answer:**

WISER is the "Wireless Information System for Emergency Responders" developed by the National Library of Medicine. This system is designed to assist first responders in hazardous material incidents. WISER provides a wide range of information on hazardous substances, including substance identification support, physical characteristics, human health information, and containment and suppression advice. (<http://wiser.nlm.nih.gov>)

**Wednesday, June 5, 2013****Question:**

Exposure to so-called skin lightening cosmetics has been associated with toxicity from what heavy metal?

**Answer:**

The cited reference notes "Use of cosmetic products containing inorganic mercury can result in systemic absorption and accumulation of mercury in the body causing renal, gastrointestinal and CNS toxicity."(Chan TYK Inorganic mercury poisoning associate with skin-lightening cosmetic products. 2011 Clin Tox 49:886-891)

**Tuesday, June 4, 2013**

**Question:**

An increased risk for which cancer has been reported with long-term use of the drug pioglitazone?

**Answer:**

The long-term use of the drug pioglitazone has been associated with the development of bladder cancer. (The Medical Letter, May 72,2013, 55(1417):42)

**Monday, June 3, 2013**

**Question:**

There are currently four dipeptidyl peptidase-4 (DPP-4) inhibitors (not formulated as drug combinations) for the treatment of type 2 diabetes currently available in the United States. These include saxagliptin (Onglyza), sitagliptin (Januvia), linagliptin (Tradjenta) and alogliptin (Nesina). What adverse effects have been associated with the use of the DPP-4 inhibitors?

**Answer:**

The adverse effects associated with the use of the DPP-4 inhibitors include acute pancreatitis, hypoglycemia when taken in combination with insulin or sulfonylureas, fatal hepatic failure, and severe hypersensitivity reactions including anaphylaxis and Stevens Johnson syndrome. The cited reference notes "the long-term safety of DPP-4 inhibitors is unknown". (The Medical Letter, May 27, 2013, 55(1417):41-43)

**Friday, May 31, 2013**

**Question:**

In 2005, a train derailment occurred near a textile mill in Graniteville, South Carolina releasing what potentially harmful chemical?

**Answer:**

This incident resulted in the release of approximately 60 tons of chlorine causing over 800 people to seek medical care. (Svendsen ER et al. Epidemiologic methods, lessons learned. 2012 Int J Env Res Pub Health 9:2894-2909)

**Thursday, May 30, 2013**

**Question:**

What is the so-called "gasping baby syndrome"?

**Answer:**

In 1982, sixteen neonatal deaths thought to be caused by the benzyl alcohol preservative used in some intravascular solutions were reported to the Food and Drug Administration (FDA). The onset of toxic illness in the infants occurred between several days and a few weeks of age with a characteristic clinical picture that included metabolic acidosis progressing to respiratory distress and gasping respirations. Many infants also had central-nervous-system dysfunction, including convulsions and intracranial hemorrhage; hypotension leading to cardiovascular collapse was a late finding usually presaging death. This came to be labelled the "gasping baby syndrome". (Neonatal deaths associated with use of benzyl alcohol-United States. 1982 MMWR, June 18, 1982, 31(22):290-291)

**Wednesday, May 29, 2013**

**Question:**

Following a therapeutic dose of acetaminophen, what percent of this drug is metabolized to NAPQI?

**Answer:**

Approximately 5 percent of acetaminophen is metabolized, via cytochrome P450 2E1, to NAPQI following therapeutic dosing. (Heard K. Acetylcysteine for acetaminophen poisoning. 2008 NEJM 359(3):285-292)

**Tuesday, May 28, 2013**

**Question:**

What is "mad honey poisoning"?

**Answer:**

According to the cited reference "mad honey poisoning" is little known outside of the country Turkey, but it is a well-described condition presenting with incapacitating and sometimes life threatening bradycardia, hypotension, respiratory depression and altered mental status. Poisoning occurs when grayanotoxin from the pollen and nectar of certain members of the family Ericaceae, especially Rhododendron L. species, enters the human food supply as "deli bah" (in Turkish) or "mad honey". (Gunduz A, et al. Clinical review of grayanotoxin/mad honey poisoning past and present. 2008 Clin Tox 46(5):437-442)

**Monday, May 27, 2013**

**Question:**

On a worldwide basis snakebite causes over 100,000 deaths each year while in the United States fatal outcomes due to reptile envenomations are an uncommon occurrence. Approximately how many deaths occur per year in the US due to reptile bites?

**Answer:**

In the United States the number of annual deaths due to reptile envenomation averages five per year. According to the cited reference, white males living in the Southern parts of the US are more likely to be victims of a fatal reptile envenomation. (Langley RL. Deaths from reptile bites in the United States, 1974-2004. 2009 Clin Tox 47(1):44-47)

**Friday, May 24, 2013**

**Question:**

Bleomycin is an anti-neoplastic drug used in the treatment of Hodgkin lymphoma, testicular cancer and Kaposi's sarcoma as well as a pleurodesis agent in malignant pleural effusions. The toxicity associated with bleomycin primarily involves skin and lungs. Pneumonitis progressing to pulmonary fibrosis is the classic lung lesion associated with bleomycin. What is the classic skin lesion attributable to bleomycin toxicity?

**Answer:**

So-called "flagellate erythema" is the classic manifestation of dermal toxicity associated with bleomycin. Flagellate erythema is an uncommon drug rash where the patient's skin has the appearance of having been repeatedly struck with a whip. The development of flagellate erythema secondary to bleomycin appear to not be dose dependent and has been reported even after the first dose of this drug. (Fyfe AJ and McKay P. Toxicities associated with bleomycin. 2010 J R Coll Physicians Edinb 40:213-215)

**Thursday, May 23, 2013**



**Question:**

What is the mechanism of action for tetrodotoxin?

**Answer:**

Tetrodotoxin selectively blocks voltage gated sodium channels. (Chau R, et al. On the origins and biosynthesis of tetrodotoxin. 2011 Aquatic Toxicology 104:61-72)

**Wednesday, May 22, 2013**

**Question:**

What is the most common clinical situation in which newborns may suffer ergot toxicity?

**Answer:**

Ergot toxicity in the newborn is virtually always due to an iatrogenic cause with an ergot drug prescribed for the mother inadvertently given to the newborn. This situation has, in the past, frequently involved an ergot compound, meant to be used as a uterotonic agent, confused with the administration of vitamin K. (Bangh SA, et al. Neonatal ergot poisoning: A persistent iatrogenic illness. 2005 Am J Perinatology 22(5):239-243)

**Tuesday, May 21, 2013**

**Question:**

What percentage of children in the US are believed to suffer from food allergies? What percentage of the children with food allergies have suffered a severe reaction requiring immediate treatment?

**Answer:**

The cited reference notes that approximately 8% of children in the United State suffer from food allergies and of these approximately 40% have a history of severe reactions requiring immediate treatment. (Gupta RS et al. Childhood food allergies: Current diagnosis, treatment and management strategies. 2013 Mayo Clin Proc 88(5): 512-526)

**Monday, May 20, 2013**

**Question:**

What is the pathophysiology of cocaine related nephropathy?

**Answer:**

While cocaine induced rhabdomyolysis is responsible for some percentage of cocaine related renal injury other mechanisms are also undoubtedly at play. The cited article notes "The pathophysiologic basis of cocaine-related renal injury is multifactorial and involves changes in renal hemodynamics, changes in glomerular matrix synthesis, degradation and oxidative stress, and induction of renal atherogenesis." (Nzerue CM et al. Cocaine and the kidney: A synthesis of pathophysiologic and clinical perspectives. 2000 Am J Kidney Dis 35: 783-795 as cited in Jaffe JA and Kimmel PL. Chronic nephropathies of cocaine and heroin abuse: A critical review. 2006 Clin J Soc Nephrol 1:655-667)

**Friday, May 17, 2013**

**Question:**

In some welding processes workers may be exposed to manganese containing fumes and some have suggested that manganese exposure may lead to the development of an atypical form of parkinsonism. Are welders at higher risk for the development of the common form of Parkinson disease?

**Answer:**

The cited reference reports a meta-analysis of 13 studies and concludes that welding and manganese exposure are not associated with an increased risk for the common form of Parkinson disease. (Mortimer JA et al. Associations of welding and manganese exposure with Parkinson disease. 2012 Neurology 79:1174-1180)

**Thursday, May 16, 2013**

**Question:**

What is the classic clinical triad associated with thallium poisoning?

**Answer:**

The classic clinical triad associated with thallium poisoning is gastroenteritis, polyneuropathy and alopecia. (Xiao T et al. Thallium pollution in China: A geo-environmental perspective. 2012 Sci Total Env 421: 51-58)

**Wednesday, May 15, 2013**

**Question:**

What is the gold or reference standard for the diagnosis of occupational asthma?

**Answer:**

The gold standard for the diagnosis of occupational asthma is specific inhalation challenge (SIC) using the suspected occupational agent at issue. (Vandenplas O, et al. Incidence of severe asthmatic reactions after challenge exposure to occupational agents. 2013 Chest 143(5):1261-1268)

**Tuesday, May 14, 2013**

**Question:**

What recently internationally banned flame retardant, widely used in polystyrene foam building insulation, is potentially toxic to aquatic life and may serve as a thyroid hormone disruptor in lab animals?

**Answer:**

Hexabromocyclodecane (HBCD) will be eliminated from worldwide production under the Stockholm Convention on Persistent Organic Pollutants by the year 2019. (Hogue C. Global ban for flame retardant. May 13,2013, Chem & Engineering News 91(19): 6)

**Monday, May 13, 2013****Question:**

The inhalation of carbon nanotubes has become a concern in the occupational setting with regard to the potential for generating pulmonary injury. What form of pulmonary injury is the primary concern regarding the inhalation of carbon nanotubes?

**Answer:**

The primary concern regarding the inhalation of carbon nanotubes is the ability for these nanoparticles to generate fibrotic reactions in the lung parenchyma. (Shevedova AA et al. Inhalation versus aspiration of single walled carbon nanotubes in C57/ B16 mice: Inflammation, fibrosis, oxidative stress and mutagenesis 2008 Am J Physiol Lung Cell Mol Physiol 295: L552-L565 as quoted in Donaldson K and Seaton A. A short history of the toxicology of inhaled particles. 2012 Particle and Fibre Toxicology 9:1-12)

**Friday, May 10, 2013****Question:**

Lionfish are common inhabitants of home and commercial aquariums. These animals can inflict severe pain that occurs rapidly following envenomation. Describe the location of the envenomating apparatus of the lionfish.

**Answer:**

According to the cited reference, “The envenomating apparatus of the lionfish consists of 12 or 13 (out of 18) dorsal spines, two pelvic spines, and three anal spines, all associated with venom glands. The pectoral spines are not associated with venom glands.” (Vetrano SJ et al. Lionfish envenomation. 2002 J Emerg Med 23(4):379-382)

**Thursday, May 9, 2013****Question:**

Tetanus is a disease caused by the toxins tetanospasmin and tetanospasmin which are elaborated by the bacterium Clostridium tetani that has been introduced as spores into injured tissue. What are the clinical characteristics of wounds considered to be “tetanus-prone”?

**Answer:**

Current thinking has tended to disregard the concept of the “tetanus-prone wound”. The cited article specifically states “The clinical determination of tetanus-prone wounds is inaccurate and seemingly trivial and non-suspicious wounds can result in tetanus. (Ataro P et al. Tetanus: A review. 2011 Southern Med J 104(8): 613-617)

**Wednesday, May 8, 2013****Question:**

Potentially fatal metabolic acidosis is the most important adverse effect due to metformin. Does this effect occur only in the overdose setting or can it also occur in the setting of therapeutic use? What is the proposed mechanism for the production of metabolic acidosis due to metformin?

**Answer:**

Potentially fatal metabolic acidosis has been reported in both the overdose and the therapeutic setting. It is posited that metabolic acidosis from metformin occurs due to the inhibition of hepatic gluconeogenesis with increased concentrations of pyruvate and alanine which also favors increased lactate formation. (Dell’Aglia DM et al. Acute Metformin Overdose: Examining Serum pH, Lactate Level, and Metformin Concentrations in Survivors Versus Nonsurvivors: A Systematic Review of the Literature. 2009 Ann Emerg Med 54:818-823)

**Tuesday, May 7, 2013****Question:**

What is the most common adverse effect of allopurinol?

**Answer:**

Skin eruption is the most common adverse effect associated with allopurinol occurring in roughly 1.5% of individuals taking this drug. These are usually simple maculopapular eruptions however very severe skin effects including DRESS, Stevens Johnson syndrome and toxic epidermal necrolysis have been reported. Allopurinol actually accounts for about 5% of these severe skin reactions. (Tsai T and Yeh T. Allopurinol in dermatology. 2010 Am J Clin Derm 11(4):225-232)

**Monday, May 6, 2013****Question:**

What are the three types of mothballs commercially available in the US? Which of these is the most commonly encountered mothball and when all three types are x-rayed which type is most radiopaque?

**Answer:**

The three types of mothballs commercially available are paradichlorobenzene (PDB), camphor, and naphthalene containing mothballs. Paradichlorobenzene containing mothballs are the most commonly used today and these (PDB) are the most radiopaque of the three groups of mothballs. (Sillery JJ et al. Hemolytic anemia induced by ingestion of paradichlorobenzene mothballs. 2009 Pediatr Emer Care 25:252-254)

**Friday, May 3, 2013****Question:**

What is considered to be the most venomous fish in the world? What types of toxins are contained in the venom of this fish? What are the clinical characteristics consistent with envenomation from this fish?

**Answer:**

The most venomous fish in the world is widely considered to be the stonefish (genus *Synanceia*). The venom includes four bio-active factors; 1- a hyaluronidase, 2-a capillary permeability factor, 3-a “lethal factor”- stonustoxin SNTX, a potent hypotensive agent with myotoxic and neurotoxic effects and 4- a pain producing factor. According to the cited reference: “Envenomation results in excruciating localized pain and gross edema which may involve the entire extremity and regional lymph nodes, peaking around 60 to 90 minutes and lasting up to 12 hours if untreated. The severity of pain may lead to unconsciousness and possible drowning. Systemic effects may include pallor, diaphoresis, nausea, muscle weakness, dyspnea, headache, and delirium: convulsions, hypotension and syncope have been reported....” (Lee JYL et al. Stonefish envenomations of the hand- A local marine hazard: A series of 8 cases and review of the literature. 2004 Ann Acad Med Singapore 33:515-520)

**Thursday, May 2, 2013****Question:**

The use of the macrolide antibiotic, azithromycin, has reportedly been associated with a 2-3 times increased risk of death from cardiovascular causes for those patients who have high pre-existing risk for death. It has been posited that this increase risk of death may be due to a proarrhythmic effect of azithromycin possibly associated with QT interval prolongation. Does azithromycin use also increase the risk for death in the general population?

**Answer:**

A recently reported study failed to demonstrate an increased risk for death due to cardiovascular causes associated with the use of azithromycin in a population of adults who were young and middle aged. (Svanstrom H et al. Use of azithromycin and death from cardiovascular causes. N Engl J Med 2013; 368:1704-1712 May 2, 2013 DOI: 10.1056/NEJMoa 1300799)

**Wednesday, May 1, 2013****Question:**

What skin lesions are associated with chronic exposure to arsenic?

**Answer:**

The skin lesions associated with chronic exposure to arsenic include “raindrop” hyperpigmentation, nonspecific hyperpigmentation, hyperkeratosis, squamous cell carcinoma, basal cell carcinoma, and Bowen’s disease. (Syed EH et al. Arsenic exposure and oral cavity lesions in Bangladesh. 2013 J Occ Env Med 55(1): 59-66)

**Tuesday, April 30, 2013****Question:**

In some cases of methamphetamine or cocaine induced hyperthermia certain morphological changes of white blood cells have been noted on the peripheral blood smear. What are these changes called and how are they described?

**Answer:**

Some cases of methamphetamine or cocaine induced hyperthermia have white blood cells with so called botryoid nuclei. These are morphological changes are sometimes seen in white blood cells and involve hyper-segmentation of the white cell nuclei with segments appearing in a radial array linked by thin filaments. The cited reference is recommended for clear images showing the characteristic appearance for botryoid nuclei. (Chew E. and Juneja S. Botryoid white cell nuclei. 2013 NEJM 368:e22 April 25, 2013 DOI: 10.1056/NEJMicm1214467)

**Monday, April 29, 2013****Question:**

Infant botulism is a rare disease with only about 100 cases annually in the United States. This disorder typically strikes children between what ages?

**Answer:**

According to the cited reference, “Infant botulism tends to strike infants between the ages of 2 and 6 months but has been reported in infants as young as 54 hours and as old as 1 year”. (Clemmens MR and Bell L. Infant botulism presenting with poor feeding and lethargy. A review of 4 cases. 2007 Pediatric Emergency Care 23(7):492-494)

**Friday, April 26, 2013****Question:**

Over the past few years, some have posited that hydraulic fracturing (fracking) operations result in elevated concentrations of what potentially explosive gas in drinking water wells in proximity to drilling operations?

**Answer:**

Methane is the potentially explosive gas that has been posited by some to be introduced into drinking water wells in proximity to fracking operations. This has created considerable controversy and many challenge the notion that this is so. (Saba T and Orzechowski M. Lack of data to support a relationship between methane contamination?of drinking water wells and?hydraulic fracturing. 2011 Proc Natl Acad Sci USA 108:8172-8176)

**Thursday, April 25, 2013****Question:**

What potentially dangerous substance is contained in the product known as Red Flower Oil?

**Answer:**

Red Flower Oil contains up to approximately 67% methyl salicylate. (Davis JE. Are one or two dangerous? Methyl salicylate exposure in toddlers. 2007 J Emerg Med 32(1): 63-69)

**Wednesday, April 24, 2013****Question:**

Protective Action Criteria or PACs are essential components for planning and response to uncontrolled releases of hazardous chemicals. During an emergency response, these criteria may be used to evaluate the severity of the event, to identify potential outcomes and to decide what protective actions may need to be taken. Which exposure limit values are the most commonly used in the derivation of PACs?

**Answer:**

The Acute Exposure Guideline Levels (AEGLs) published by the US EPA, the Emergency Response Planning Guidelines (ERPGs) produced by the American Industrial Hygiene Association and the Temporary Emergency Planning Exposure Limit (TEELs) developed by the Subcommittee on Consequence Assessment and Protective Actions (SCAPA) are the exposure limit values most commonly used as PACs. (<http://orise.orau.gov/emi/scapa/chem-pacs-teels/default.htm>)

**Tuesday, April 23, 2013****Question:**

What is the so-called “cinnamon challenge”?

**Answer:**

According to the cited article, the “cinnamon challenge”, an evolving adolescent fad, involves “swallowing a tablespoon of ground cinnamon in 60 seconds without drinking fluids. However, as stated on [www.cinnamonchallenge.com](http://www.cinnamonchallenge.com), this challenge is practically impossible, decidedly unpleasant, and potentially harmful.” The authors further point out that ingesting cinnamon powder may increase the risk for aspiration and that cinnamon inhalation may result in pulmonary inflammation and thus to airway damage and potentially aspiration pneumonia. (Grant-Alfieri A, Schaechter J and Lipshultz S E. Ingesting and aspirating dry cinnamon by children and adolescents: The 'Cinnamon Challenge'. 2013 Pediatrics 131(5): 833-835)

**Monday, April 22, 2013****Question:**

Based on recent reports, clinicians caring for otherwise healthy adolescents and young adults with unexplained acute kidney injury (AKI) should inquire about use of what hallucinogens?

**Answer:**

Clinicians caring for otherwise healthy adolescents and young adults with unexplained acute kidney injury (AKI) should inquire about the use of synthetic cannabinoids. These substances have recently been noted to be associated with the development of AKI however the precise mechanism for this effect is yet to be proven. (MMWR February 5, 2013. Acute kidney injury associated with synthetic cannabinoid use- Multiple states 2012. 62(6): 93-98)

**Friday, April 19, 2013****Question:**

Lindane (gamma-hexachlorocyclohexane) is a chlorinated hydrocarbon that has been used as a human scabicide and anti-lousing agent. The use of this agent has been reported to be associated with significant human toxicity in some cases. Is most of the serious toxicity associated with lindane related to the proper, labeled use or due to excessive and inappropriate use of lindane?

**Answer:**

The authors for the cited reference report the results of an extensive literature search and they note “Although the majority of deaths associated with lindane were due to excessive use (> one 4-minute application of shampoo or > 8 to 12 hours of a single total body application of lindane lotion 1%), the majority of patients reporting seizures and respiratory problems had used the labeled dose. Moreover, ingestions of lindane were extremely rare.” (Nolan K et al. Lindane toxicity: A comprehensive review of the medical literature. 2012 Pediatr Derm 29(2):141-146)

**Thursday, April 18, 2013****Question:**

What is the mechanism of the acute toxicity associated with exposure to the insecticide chlorpyrifos?

**Answer:**

Chlorpyrifos is an organophosphate insecticide and as such acts as a cholinesterase inhibitor. This primary acute toxic effect of chlorpyrifos is related to the formation of chlorpyrifos-oxon the active metabolite of chlorpyrifos that acts to irreversibly inhibit the activity of cholinesterase. (Zhao Q et al. A review of the reference dose for chlorpyrifos. 2006 Regulatory Toxicology and Pharmacology 44:111–124)

**Wednesday, April 17, 2013****Question:**

Indigenous U.S. coral snakes occur naturally in 11 states. Which states?

**Answer:**

Micrurus fulvius occurs naturally in portions of North Carolina, South Carolina, Georgia, Florida, Alabama, Mississippi and Louisiana east of the Mississippi River. Micrurus tener occurs naturally in Louisiana west of the Mississippi River and in parts of Texas and Arkansas. Micruroides euryxanthus occurs naturally in parts of Arizona and New Mexico. (Walter F., et al. Temporal analysis of coral snakebite severity published in the American Association of Poison Control Centers' Annual Reports from 1983—2007. 2010 Clin Tox 48:72-78)

**Tuesday, April 16, 2013****Question:**

What potentially dangerous gas results from the combustion of polyvinyl chloride?

**Answer:**

Phosgene is produced when polyvinyl chloride burns. (Toon MH et al. Management of acute smoke inhalation. 2010 Crit Care Resusc 12:53-61)

**Monday, April 15, 2013****Question:**

What are the TEELs?

**Answer:**

TEELs are “Temporary Emergency Exposure Limits” and are currently designated for approximately three thousand different chemicals. TEELs are designed to be temporary guidelines generally applied to acute chemical release incidents. They are applied only in cases where Acute Exposure Guideline Levels (AEGs) or Emergency Response Planning Guidelines (ERPGs) have yet to be developed for a given chemical. (U.S. Department of Energy (2008). Temporary Emergency Exposure Limits for Chemicals: Methods and Practice. Washington, D.C.)

**Friday, April 12, 2013****Question:**

What are the characteristics of the retinal toxicity associated with hydroxychloroquine and chloroquine?

**Answer:**

The retinal toxicity associated with hydroxychloroquine and chloroquine begins as paracentral scotomata. These findings are usually evident on visual field testing even before changes in the appearance of the ocular fundus are seen. The authors of the cited article point out that if “the toxic drug is stopped before fundus changes occur, the scotomata can resolve” in many but not all cases. However, once fundus changes occur, the scotomata usually will not resolve and may actually get worse even after cessation of the drug. (Browning DJ. Hydroxychloroquine and chloroquine retinopathy: Screening for drug toxicity. 2002 Am J Ophthalmol 133:649-656)

**Thursday, April 11, 2013****Question:**

Pentachlorophenol (PCP) is a chlorinated aromatic compound that is highly lipid soluble. PCP has been used primarily as a wood preservative but has also found use as an herbicide, insecticide, and molluscicide. What are the clinical hallmarks of acute poisoning with this substance and what is the most likely toxic mechanism of action?

**Answer:**

The hallmarks of acute poisoning with pentachlorophenol include altered mental status, seizures, tachycardia, tachypnea, associated with pulmonary edema, intravascular hemolysis, pancreatitis and/or acute renal failure. The most likely mechanism of acute toxicity is uncoupling of oxidative phosphorylation as PCP has been shown to bind to mitochondria and to induce structural changes in mitochondria. (Proudfoot AT. Pentachlorophenol poisoning. 2003 Toxicol Rev 22(10): 3-11)

**Wednesday, April 10, 2013****Question:**

What are the constituents of diesel exhaust?

**Answer:**

The cited authors note “Diesel exhaust is a complex mixture of particulate matter and gases, and includes particles less than 1.0 mm in diameter with mutagenic and polycyclic aromatic hydrocarbon (PAH) [potentially] carcinogenic compounds adsorbed to a carbon core and ultrafine particles made up of condensed organics.” (Kittelson D, et al. Measurement of diesel aerosol exposure: a feasibility study. In: Diesel Epidemiology Working Group, editor. Research directions for improved estimates of human exposure and risk from diesel exhaust. Boston, MA: Health Effects Institute; 2002 as cited in Hart JE et al. Occupational diesel exhaust exposure as a risk factor for chronic obstructive pulmonary disease. 2012 Curr Opin Pulm Med 18:151-154)

**Tuesday, April 9, 2013****Question:**

What is the CAS REGISTRY? What is a CAS Registry Number (CAS RN)?

**Answer:**

The CAS REGISTRY is an authoritative collection of disclosed chemical substance information, containing more than 71 million organic and inorganic substances and 64 million sequences. The CAS REGISTRY covers substances identified from the scientific literature from 1957 to the present, with additional substances going back to the early 1900s. Each CAS Registry Number (often referred to as a CAS Number): 1- Is a unique numeric identifier; 2- Designates only one substance; 3- Has no chemical significance; 4- is a link to a wealth of information about a specific chemical substance. (<http://www.cas.org/content/chemical-substances/faqs#q1>)

**Monday, April 8, 2013****Question:**

What is RTECS?

**Answer:**

RTECS is the “Registry of Toxic Effects of Chemical Substances”, a definitive toxicological database with supplemental information pertinent to both the chemical industry and the occupational safety and health community. This technical data may be helpful to assess workers’ exposures to chemicals, particularly to lesser-known-and-used chemical substances. OSHA has designated RTECS as a primary source for toxicity data for Material Safety Data Sheets in its Hazard Communications Rule. In recent years RTECS has grown to include more than 160,000 chemicals. The toxicological data are organized into six fields: primary irritation, mutagenic effects, reproductive effects, tumorigenic effects, acute toxicity and multiple dose toxicity. Each data line includes the citation to its bibliographic source. RTECS provides a host of reference data including, but not limited to: CAS Numbers, OSHA PELs, ACGIH TLVs, NIOSH RELs, Carcinogenic assessments, Beilstein Reference Numbers, and Bioassay results from the National Toxicology Program. (<http://www.cdc.gov/niosh/rtecs/RTECSfeatures.html>)

**Friday, April 5, 2013****Question:**

What is yohimbine? What is its mechanism of action and what are the most common clinical findings associated with yohimbine overdose?

**Answer:**

Yohimbine is an indole alkaloid derived from a wide variety of plant sources including Rauwolfia root as well as the bark of the Pausinystalia yohimbe tree. Yohimbine acts as a competitive antagonist selective for alpha-2 adrenergic receptors. It may also interact with alpha-1- adrenoreceptors, serotonin and dopamine receptors. The authors for the cited article note that the most common clinical findings associated with yohimbine overdose are “skin flushing, vasodilation, tachycardia, hypertension, GI distress, anxiety, irritability, tremor, dizziness, headache and hallucinations”. (Giampreti A, et al. Acute neurotoxicity after yohimbine ingestion by a body builder. 2009 Clin Tox 47:827-829)

**Thursday, April 4, 2013**

**Question:**

What is green tobacco illness?

**Answer:**

Green tobacco sickness (GTS) is an occupational disease caused by nicotine poisoning that occurs secondary to dermal absorption of dissolved nicotine on tobacco plants. This affliction may be seen in tobacco workers (including child workers) who come into direct contact with wet tobacco plants typically occurring during the process of tobacco harvesting. Individuals with GTS may present with a variety of symptoms consistent with nicotine poisoning including weakness, headache, nausea, vomiting, dizziness, crampy abdominal pain, difficulty breathing, pallor, diarrhea, chills, hypotension/hypertension, bradycardia/tachycardia, and increased perspiration and salivation. The onset of GTS ranges from 3 to 17 hours after exposure and the duration of illness is typically from one to three days. (McBride J, et al. Green tobacco sickness. 1998 Tobacco Control 7:294-298)

**Wednesday, April 3, 2013**

**Question:**

What is “fire eater’s lung”? What substances are most commonly causally implicated in this occupational illness and what are the clinical characteristics associated with this problem?

**Answer:**

The cited reference notes “fire-eater’s pneumonia (or lung) is an acute exogenous lipid pneumonia that may develop among regular practitioners of fire-eating.” The authors point out: “The substances most commonly used during fire-eating are kerdan and liquid paraffin (kerosene). If aspirated, these substances may rapidly diffuse into the bronchial tree, causing acute chemical pneumonitis. The first symptoms usually appear within 12 h and consist of high fever, cough, dyspnoea and chest pain. Haemoptysis has also been observed. Laboratory findings generally include increased CRP levels and leucocytosis. A drop in SaO<sub>2</sub> has been described in some cases. Early CXR typically reveal unilateral or bilateral alveolar infiltrates in the middle or lower regions of the lungs, often accompanied by hilar lymphadenopathy.” (Harlander M et al. Fire-eater’s lung complicated by an infectious abscess requiring surgical treatment. 2010 Respirology 15(2): 379-381)

**Tuesday, April 2, 2013**

**Question:**

In which industries might workers be exposed to antimony?

**Answer:**

The cited reference points out that “workers involved in industries producing antimony and antimony trioxide, metal mining, smelting and refining, coal-fired power plants, refuse incineration, or those working in indoor firing ranges” are the most likely to have occupational exposure to antimony. The authors further indicate “Most of the data of antimony toxicity comes from the time when primitive work conditions prevailed and there was no adequate protection for the workers. Another problem in assessing its toxicity industrially is that arsenic and lead are often found with it, and other toxic materials may also be produced in the course of the process, and separation of exposures may be difficult or impossible.” (Sundar S and Chakravarty J. Antimony toxicity 2010 Int. J. Environ. Res. Public Health, 7:4267-4277)

**Monday, April 1, 2013**

**Question:**

Exposure to UV-A and UV-B radiation are risk factors for the development of which ocular diseases?

**Answer:**

Exposure to UV-A and UV-B radiation are risk factors for the development of macular degeneration and cataract formation. (Roberts J E. Ultraviolet radiation as a risk factor for cataract and macular degeneration. 2011 Eye & Contact Lens 37(4): 246-249)

**Friday, March 29, 2013**

**Question:**

Q fever, caused by *Coxiella burnetii*, is designated by the CDC as a biological threat agent. However, this disease is also considered an occupational disease. In which occupations might workers be at risk to develop Q fever?

**Answer:**

According to a recent MMWR publication “Q fever is an occupational disease in persons whose work involves contact with animals, such as slaughterhouse workers, veterinarians, and farmers, although infection is not limited to these groups. Urban outbreaks and cases with no known exposure or close proximity to livestock have been reported, as have nonoccupational exposures such as through a hobby farm (a small farm that is not a primary source of income)”. (Diagnosis and management of Q fever- United States, 2013: Recommendations from CDC and the Q fever working group. March 29, 2013 MMWR 62(RR03): 1-23)

**Thursday, March 28, 2013**

**Question:**

What chemical, used by some to promote weight loss and marketed via the internet under the names ‘Dinosan’, ‘Dnoc’, ‘Solflo Black’, ‘Nitrophen’, ‘Aldifen’ and ‘Chemox’ was first used by the French in munitions production during World War I?

**Answer:**

Dinitrophenol (DNP), which acts by uncoupling oxidative phosphorylation, has been sold on internet sites under the names ‘Dinosan’, ‘Dnoc’, ‘Solflo Black’, ‘Nitrophen’, ‘Aldifen’ and ‘Chemox’ and marketed for weight loss purposes. It is important to note that the use of DNP for weight loss has resulted in significant and severe adverse effects including death. (Grundlingh J et al. 2,4-Dinitrophenol (DNP): A weight loss agent with significant acute toxicity and risk of death 2011 J Med Toxicol 7:205-212)

**Wednesday, March 27, 2013**

**Question:**

BEIs are one guideline used to assist in the control of potential health hazards associated with exposure to chemicals. What are the BEIs and what organization develops and promulgates these particular guidelines?

**Answer:**

BEIs are “Biological Exposure Indices” and are developed and promulgated by the ACGIH (American Conference of Governmental Industrial Hygienists). (2013 TLVs and BEIs. ACGIH, Cincinnati, Ohio)

**Tuesday, March 26, 2013****Question:**

Anthracycline drugs (e.g. doxorubicin and daunorubicin) are used to treat a variety of cancers. These drugs are associated with what cardiovascular complication and for how long must these drugs be used before this toxicity develops?

**Answer:**

Anthracycline drugs are associated with an increased risk for congestive heart failure. The cited authors note “the risk (of heart failure) [is] proportionate to the cumulative exposure; cardiac injury appears to occur with every dose, and cardiac-biopsy specimens obtained within hours after a single dose of an anthracycline show pathologic changes.” (Unverferth BJ, et al. Early changes in human myocardial nuclei after doxo- rubicin. Cancer 1983;52:215-21 as cited in Sawyer DB Anthracyclines and heart failure. 2013 NEJM 368:12)

**Monday, March 25, 2013****Question:**

What toxin has been shown to be the cause for so-called Balkan endemic nephropathy?

**Answer:**

Balkan endemic nephropathy is caused by ingestion of aristolochic acid, usually contained in herbal or other home remedies. Aristolochic acids are chemicals found in the Aristolochia genus of plants. This form of renal disease is also known as aristolochic acid nephropathy (AAN). The authors of the cited reference note AAN is characterized by “extensive interstitial fibrosis associated with tubular atrophy and low numbers of chronic inflammatory cells decreasing from the outer to the inner cortical labyrinth”. They go on to point out “Virtually all patients have associated multifocal urothelial atypia, and 40% to 46% of patients have multifocal, often bilateral transitional cell carcinoma in situ, usually located in the upper urinary tract.” (Gokmen MR et al. The epidemiology, diagnosis and management of aristolochic acid nephropathy. 2013 Ann Intern Med 158:469-477)

**Friday, March 22, 2013****Question:**

What is Kratom and what is its major constituent?

**Answer:**

Mitragyna speciosa, also known as Kratom, is a tree that is native to some swamps of Asia and Africa. At moderate doses, Kratom has been used for its stimulant effects. At higher doses, Kratom reportedly exhibits opioid effects. Over 20 alkaloids have been isolated from Kratom with mitragynine noted to be the major alkaloid constituent and the one likely responsible for the opioid effects associated with Kratom. (Babu K et al. Opioid receptors and legal highs: Salvia divinorum and Kratom. 2008 Clin Tox 46:146-152)

**Thursday, March 21, 2013****Question:**

What is the rate of fatal hemorrhage among patients taking warfarin? What is the most commonly used agent for warfarin reversal?

**Answer:**

Fatal hemorrhage reportedly occurs at the rate of approximately 1% per year among patients taking warfarin. The cited reference notes that while reversal may be accomplished using a variety of agents, approximately 60% of all units of fresh frozen plasma (FFP) transfused each year are used for the reversal of warfarin making FFP the currently most frequently used reversal agent for warfarin. (Rashidi A and Tahhan HR. Fresh frozen plasma dosing for warfarin reversal: A practical formula. 2013 Mayo Clin Proc 88(3):244-250)

**Wednesday, March 20, 2013****Question:**

What are the sources for radiation exposure that may occur via drinking water?

**Answer:**

The cited reference notes “Radiation exposure through drinking water results from naturally occurring radionuclides in drinking water sources, in particular alpha- radiation–emitting uranium, radium, and their progeny, including radon.” (Canu IG et al. Health effects of naturally radioactive water ingestion: The need for enhanced studies. 2011 Environ Health Perspect 119:1676-1680)

**Tuesday, March 19, 2013****Question:**

What is the potential for genotoxicity associated with exposure to the herbicide glyphosate and related glyphosate-based formulation (GBF) herbicides?

**Answer:**

The cited reference indicates “Reports of positive results for DNA damage endpoints indicate that glyphosate and GBFs tend to elicit DNA damage effects at high or toxic dose levels, but the data suggest that this is due to cytotoxicity rather than DNA interaction with GBF activity perhaps associated with the surfactants present in many GBFs. Glyphosate and typical GBFs do not appear to present significant genotoxic risk under normal conditions of human or environmental exposures.” (Kier LD and Kirkland DJ. Review of genotoxicity studies of glyphosate and glyphosate-based formulations. 2013 Crit Rev in Toxicol, early online: 1-33. <http://informahealthcare.com/doi/pdf/10.3109/10408444.2013.770820>)

**Monday, March 18, 2013****Question:**

What are the toxicologically related risk factors for the development of thrombotic thrombocytopenic purpura (TTP)?

**Answer:**

The toxicologically related risk factors for the development of TTP include infection with Shiga toxin–producing *Escherichia coli* (STEC) and the use of drugs, including platelet aggregation inhibitors, quinine, and cocaine. More recently cases of TTP have been reported to be associated with dissolving and injecting tablets of Opana ER (Endo Pharmaceuticals), a recently reformulated extended-release form of oxycodone intended for oral administration. (Thrombotic Thrombocytopenic Purpura (TTP)–Like Illness Associated with Intravenous Opana ER Abuse — Tennessee, 2012 MMWR January 11, 2013 / 62(01);1-4)

**Friday, March 15, 2013****Question:**

Chronically elevated serum levels of fluoride are associated with what radiological findings in the vertebral bodies as seen on plain x-ray?

**Answer:**

Skeletal fluorosis may be associated with the so-called “rugger jersey sign”, a pattern of vertical striations reflecting increased bone density in the upper and lower areas of the vertebral bodies. Skeletal fluorosis occurs in geographic areas where high levels of fluoride exist in drinking water. (Image Challenge 2013 NEJM March 14, 2013 online at <http://www.nejm.org/image-challenge>)

**Thursday, March 14, 2013****Question:**

What is the risk for developing ischemic heart disease in women who have received radiotherapy for breast cancer?

**Answer:**

The authors of a recent population based study of females who were treated with radiotherapy for breast cancer concluded: “Exposure of the heart to ionizing radiation during radiotherapy for breast cancer increases the subsequent rate of ischemic heart disease. The increase is proportional to the mean dose to the heart, begins within a few years after exposure, and continues for at least 20 years. Women with preexisting cardiac risk factors have greater absolute increases in risk from radiotherapy than other women.” (Darby SC et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. 2013 NEJM 368:987-998)

**Wednesday, March 13, 2013****Question:**

What is the mechanism of action for misoprostol (Cytotec and generics) when prescribed for miscarriage?

**Answer:**

The cited reference points out that “misoprostol binds to myometrial cells and induces uterine contractions”. (The Medical Letter, March 4, 2013, 55(1411):19-20)

**Tuesday, March 12, 2013****Question:**

What is the general accuracy of electronic databases used by clinicians and others to check for drug-drug interactions (DDIs)?

**Answer:**

The cited reference reports “Of several software systems evaluated, most were unable to detect 50% of DDIs and one program left 77% of DDIs undetected”. The authors note that another study (Yap) of four major drug databases evaluated reported accuracy rates were as follows: “34% Drugs.com; Medscape 18%; Drug Digest 8% and Micromedex 56%”. The authors further note “despite this lack of accuracy, these databases are widely used and may be viewed as a criterion standard....” (Seminario MJ and Retain MJ Preventing adverse drug-drug interactions: A need for improved data and logistics” 2013 Mayo Clin Proc 88(2):126-128 and Yap KY et al. OncoRx-IQ: a tool for quality assessment of online anticancer drug interactions. 2010 22(2):93-106)

**Monday, March 11, 2013****Question:**

What is the primary toxin in Portuguese man-of-war venom?

**Answer:**

The primary toxin in Portuguese man-of-war venom is Physaliatoxin. This is a 240 kDa glycoprotein and is a potent hemolytic and cytotoxic agent. (Labadie M, et al. Portuguese man-of-war (Physalia physalis) envenomation on the Aquitaine Coast of France: An emerging health risk. 2012 Clin Tox 50(7):567-570)

**Friday, March 8, 2013****Question:**

What are the common sources for polycyclic aromatic hydrocarbons (PAHs)?

**Answer:**

Polycyclic aromatic hydrocarbons (PAHs) are a group of over 100 different chemicals that are formed during the incomplete burning of coal, oil and gas, garbage, or other organic substances like tobacco or charbroiled meat. PAHs are usually found as a mixture containing two or more of these compounds, such as soot. In addition, some PAHs are manufactured. These pure PAHs usually exist as colorless, white, or pale yellow-green solids. PAHs are found in coal tar, crude oil, creosote, and roofing tar, but a few are used in medicines or to make dyes, plastics, and pesticides. (<http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=25>)

**Thursday, March 7, 2013****Question:**

What is the EPA National Priorities List (NPL)?



**Answer:**

The National Priorities List (NPL) is the list of national priorities among the known releases or threatened releases of hazardous substances, pollutants, or contaminants throughout the United States and its territories. The NPL is intended primarily to guide the EPA in determining which sites warrant further investigation. (<http://www.epa.gov/superfund/sites/npl/index.htm>)

**Wednesday, March 6, 2013**

**Question:**

Pneumomediastinum has been reported as a result of crack cocaine use by inhalation. What is the recommended treatment for cocaine related pneumomediastinum?

**Answer:**

The complication of cocaine-induced pneumomediastinum is generally considered to be self-limited and relatively benign. The cited reference recommends: "When patients present with mild symptoms and no associated pneumothorax, a short observation period in the emergency room or hospital ward is sufficient in most cases. Intensive care unit admission is not usually necessary. When patients are admitted, hospital discharge should not be delayed pending radiological resolution. Patients with a stable or improved follow-up chest radiograph can be safely discharged and followed up as an outpatient. The majority of patients who present with cocaine-induced pneumomediastinum and concomitant pneumothorax can be managed conservatively without thoracostomy tube drainage." (Alnas M et al. Clinical course and outcome of cocaine-induced pneumomediastinum. 2010 Am J Med Sci 339(1):65-67)

**Tuesday, March 5, 2013**

**Question:**

Talc retinopathy is related to intravenous drug use in some cases. What is the nature of this association?

**Answer:**

According to the cited reference: "Talc is an inert filler in methylphenidate hydrochloride tablets, which are crushed for intravenous drug use. The talc is then unknowingly injected intravenously. Talc particles are usually fine and are distributed intravascularly and extravascularly in the retina in patients who chronically use intravenous drugs and in whom right-to-left cardiopulmonary shunting occurs through collateral vessels that may develop around sites of pulmonary infarction. However, in a patient with a patent foramen ovale, larger particles may cause retinal artery occlusions and severe vision loss." (Schoenberger SD and Agarwal A. Talc Retinopathy. 2013 NEJM 368:852)

**Monday, March 4, 2013**

**Question:**

More than 50% of all pregnant females experience nausea and vomiting during their pregnancy. Ondansetron is often used to treat these symptoms. Is ondansetron safe to use during pregnancy?

**Answer:**

A recent study evaluating a cohort of more than 600,000 pregnancies reported that ondansetron was "not associated with an increased risk of adverse fetal outcomes". (Pasternak B et al. Ondansetron in pregnancy and risk of adverse fetal outcomes. 2013 NEJM 368(9):814-823)

**Friday, March 1, 2013**

**Question:**

Body piercing is a risk factor for the development of hypersensitivity to what material?

**Answer:**

Body piercing is a risk factor for the development of hypersensitivity to nickel, which is commonly a major component of the jewelry used in body piercing. The cited reference notes that the prevalence of nickel hypersensitivity in the face of body piercing increases with increasing numbers of body piercings. Body piercings are thought to significantly contribute to the fact that the rate of nickel appears to be increasing in North America. (Schram SE et al. Nickel hypersensitivity: a clinical review and call to action. 2010 Int J Derm 49:115-125)

**Thursday, February 28, 2013**

**Question:**

What are typical findings with regard to platelet counts in cases of heparin-induced thrombocytopenia?

**Answer:**

In the face of heparin-induced thrombocytopenia, platelet counts are typically only moderately decreased. In some cases, patients may not demonstrate absolute thrombocytopenia, but have platelet counts that are decreased by approximately 50% from pre-heparin administration levels. (Kelton JG et al. Nonheparin anticoagulants for heparin-induced thrombocytopenia. 2013 NEJM 368:737-744)

**Wednesday, February 27, 2013**

**Question:**

What are the two currently approved prescription cannabinoids available in the US and what indications are they currently approved for?

**Answer:**

The cited reference notes that there are two prescription cannabinoids currently available, Marinol (dronabinol; a synthetic  $\Delta^9$ -THC) and Cesamet (nabilone; a  $\Delta^9$ -THC congener). These drugs are approved by the FDA for the treatment of nausea and vomiting associated with the administration of chemotherapeutic agents. (Reisfield GM and DuPont RL. Recommend against the medicinal use of marijuana. 2013 NEJM February 20, 2013, Online First, DOI: 10.1056/NEJMc1300970)

**Tuesday, February 26, 2013**

**Question:**

What liver condition, characterized by diffuse blood filled lesions, ectatic veins and widely dilated hepatic sinusoids is associated with androgen therapy?

**Answer:**

The liver condition characterized by diffuse blood filled lesions, ectatic veins and widely dilated hepatic sinusoids associated with androgen therapy is known as peliosis hepatis. (Walter E and Mockel J. Peliosis hepatis 1997 NEJM 337(220:1603)

**Monday, February 25, 2013****Question:**

What is orpiment?

**Answer:**

Orpiment is inorganic arsenic trisulfide. The cited reference notes that orpiment is a naturally occurring mineral, known for its bright yellow color, often found near volcanic formations and also as a coal combustion byproduct. This arsenical material is a poorly soluble inorganic form of arsenic and, as such, may not pose a serious health threat following ingestion. In fact, the cited reference reports the management of a massive ingestion of orpiment without the use of chelation medications. (Buchanan JA et al. Massive human ingestion of orpiment (arsenic trisulfide) 2013 J Emerg Med 44(2):367-372)

**Friday, February 22, 2013****Question:**

A new epinephrine auto-injector has recently been marketed under the name Auvi-Q. How does Auvi-Q differ from the traditional EpiPen?

**Answer:**

The cited reference points out that Auvi-Q is smaller than the traditional EpiPen in that Auvi-Q is “about the length and width of a credit card and as thick as a smart phone”. In addition, when activated the Auvi-Q device actually provides real time audio instructions for use followed by a 5 second delay to injection of drug. Epinephrine levels following Auvi-Q use are similar to those of the EpiPen. (The Medical Letter, February 18,2013 55(1410):13)

**Thursday, February 21, 2013****Question:**

Proton pump inhibitors (PPIs) have been associated with an increased risk of fractures with long-term use. What is the proposed mechanism for this adverse effect of PPI's?

**Answer:**

The cited reference notes “Possible connections between PPIs and fracture risk include inhibition of gastric acid secretion which might interfere with absorption of calcium and interference with the activity of osteoclasts which could lead to a decrease in bone resorption.” (The Medical Letter February 18,2013, 55(1410):15-16)

**Wednesday, February 20, 2013****Question:**

What essentially benign ocular changes may be associated with the use of prostaglandin analogue eye drops in the treatment of glaucoma?

**Answer:**

Benign hyperpigmentation of the iris may occur in certain susceptible individuals using prostaglandin analogue drops to treat chronic open angle glaucoma. The cited reference notes “Those most vulnerable to iris color change are patients with hazel eyes either green brown, golden brown or, to a lesser extent, blue brown.” (Grierson I et al. The iris after prostanoïd treatment. 2001 Curr Opinion in Ophthalmology 12:112-118)

**Tuesday, February 19, 2013****Question:**

Following death, to what degree does the decomposition of the human body generate detectable blood ethanol levels?

**Answer:**

According to the cited reference, “the data are consistent with previous studies and suggest that decomposition is rarely an important factor in causing blood ethanol concentrations above 70 mg%, but further study needs to be undertaken.” (Hanzlick R. Ethanol concentration in decomposing bodies: Another look, less concern. Letter to the Editor, 2009 Am J For Med and Path, 30(1): 88)

**Monday, February 18, 2013****Question:**

What are the common problems associated with pediatric ingestion of magnetic foreign bodies?

**Answer:**

When two or more magnetic foreign bodies are attracted to each other across bowel walls in the GI tract, the most common problems involve local pressure necrosis with the subsequent development of small bowel obstruction, volvulus, fistula formation or bowel perforation. (Tavarez M et al. Prevalence, clinical features and management of pediatric magnetic foreign body ingestions. 2013 J Emerg Med 44(1):261-268)

**Friday, February 15, 2013**

**Question:**

What is the most frequently used alternative medicine for hepatic disease in the United States today?

**Answer:**

Silymarin is the most frequently used alternative medicine for hepatic disease in the United States today. (National Center for Complimentary and Alternative Medicine as cited in Ward J et al. Amatoxin poisoning: Case reports and review of current therapies. 2013 J Emerg Med 4491):116-121)

**Thursday, February 14, 2013****Question:**

What is “vineyard sprayer’s lung”?

**Answer:**

Vineyard sprayer’s lung (VSL) is a “vintage” occupational disease first described in 1969. VSL was reported to result from the inhalation of quantities of Bordeaux mixture that was sprayed in vineyards to combat grape mildew. Bordeaux mixture contained copper sulfate neutralized with hydrated lime. This inhalation exposure resulted in severe granulomatous pulmonary disease. (Pimentel J and Marques F. Vineyard sprayers lung: a new occupational disease. 1969 Thorax 24:678-688)

**Wednesday, February 13, 2013****Question:**

What is the most common solvent used in the dry cleaning industry worldwide?

**Answer:**

Tetrachloroethylene is the most common solvent used in the dry cleaning industry on a worldwide basis. (Lyng E. et al. Exposure to tetrachloroethylene in dry cleaning shops in the Nordic countries. 2011 Ann. Occup. Hyg., 55(4): 387–396

**Tuesday, February 12, 2013****Question:**

In 1943, during World War II, an air raid attack against Allied ships moored at Bari, Italy, resulted in the release of what poisonous material being stored on at least one of these ships?

**Answer:**

The US Liberty ship John Harvey contained secret stores of sulfur mustard in 2000 bombs. Large quantities of sulfur mustard were release into the water as well as into the atmosphere causing large numbers of casualties. (Reminick, Gerald (2001). Nightmare in Bari: The World War II Liberty Ship Poison Gas Disaster and Coverup. Palo Alto: Glencannon Press. ISBN 1-889901-21-0.)

**Monday, February 11, 2013****Question:**

Specific pneumococcal vaccines are recommended for infants, children, certain immunocompromised adults, and individuals older than 65 years of age. What toxicity is associated with the pneumococcal vaccines currently available in the United States?

**Answer:**

While pneumococcal vaccines may be associated with local redness, swelling and pain, the currently available pneumococcal vaccines have not been associated with any significant systemic toxicity to date. (The Medical Letter October 29,2012, 54(1402): 87)

**Friday, February 8, 2013****Question:**

How quickly does non-cardiogenic pulmonary edema related to heroin overdose develop?

**Answer:**

Non-cardiogenic pulmonary edema related to heroin overdose is an uncommon complication of heroin overdose. Most authorities report that this phenomenon occurs within 4 hours of the overdose with many cases occurring immediately following the overdose. Clinicians should be aware of the potential for delayed onset of this problem (Sporer KA and Dorn E. Heroin-related non-cardiogenic pulmonary edema : a case series. 2001 Chest 120(5):1628-1632)

**Thursday, February 7, 2013****Question:**

What is the so-called “Nazi method” for producing illicit methamphetamine?

**Answer:**

The clandestine manufacture of methamphetamine by the use of excess alkali metal (e.g. lithium) in liquid ammonia is commonly referred to as the “Nazi method.” Also known as the Birch reduction method. This method is so named because it is the method used by the Nazis in World War II to produce methamphetamine (Pal R, et al. Fate of 1-(1',4'-cyclohexadienyl)-2-methylaminopropane (CMP) in soil: Route-specific by-product in the clandestine manufacture of methamphetamine. 2012 Sci Total Env 416:394-399)

**Wednesday, February 6, 2013****Question:**

Occupational exposure to vinyl chloride has been associated with the development of hepatic angiosarcoma. How many cases of this disease occur in the US on an annual basis?

**Answer:**

Hepatic angiosarcoma is a very rare disease. Approximately 20-30 cases are reported in the US on an annual basis. (Toxicological Review of Vinyl Chloride. EPA May, 2000)

**Tuesday, February 5, 2013****Question:**

In the infamous 1995 Tokyo terrorist release of sarin there were 640 victims who arrived at the St Luke's Hospital after the incident. Of these, 111 were admitted to the hospital. What was the most common physical finding in the sarin nerve agent victims who were admitted to hospital?

**Answer:**

Miosis was the most common finding in those individuals who were admitted to St Luke's Hospital following the Tokyo sarin nerve agent incident. Miosis was identified in 99% of these admitted patients. (Yanagisawa N et al. Sarin experiences in Japan: Acute toxicity and long term effects. 2006 J Neurol Sci 249:76-85)

**Monday, February 4, 2013****Question:**

Isotretinoin (Accutane) is extremely effective as an acne treatment. What is the pregnancy category for isotretinoin?

**Answer:**

Isotretinoin is noted to be a potent human teratogen and is rated as pregnancy category X. (The Medical Letter; January 21, 2013, 55(1408):8)

**Friday, February 1, 2013****Question:**

What is the proposed pathogenesis for hypoglycemia associated with ethanol intoxication?

**Answer:**

The pathogenesis for this phenomenon has not been proven but is likely a result of the inhibition of hepatic gluconeogenesis. The cited reference notes "Ethanol metabolism increases the nicotinamide adenine dinucleotide (NADH-NAD) ration as the NAD is depleted and interferes with the formation of glucose from its precursors." These authors point out that this phenomenon is more likely in individuals with reduced hepatic reserves of glycogen such as young children, under nourished individuals and people on extreme weight reduction diets. (Vogel C, et al. Alcohol intoxication in young children. 1995 Clin Tox 33(1):25-33)

**Thursday, January 31, 2013****Question:**

Why has the FDA recently required manufacturers of zolpidem-containing products (Ambien, Ambien-CR, Edluar, and Zolpimist) to lower dose recommendations?

**Answer:**

FDA has recommended lower doses of zolpidem containing drugs as a result of driving simulations that found that serum levels of zolpidem greater than 50ng/mL can adversely impact driving performance. The cited reference points out that recent studies have shown that "8 hours after taking 10 mg Ambien, 15% of women and 3% of men had serum concentrations of zolpidem >50 ng/mL. With extended-release zolpidem 12.5 mg, 33% of women and 25% of men had serum concentrations greater than 50 ng/mL 8 hours after taking the drug." (The Medical Letter, January 21, 2013, 55(1408):5)

**Wednesday, January 30, 2013****Question:**

Palytoxin was first isolated in the early 1970s from certain species of soft coral. It has also been found in dinoflagellates (genus *Ostreopsis*). How might humans be impacted by exposure to palytoxins?

**Answer:**

Palytoxins are marine toxins believed to be concentrated up the food chain. They have been identified in a variety of fish, mollusks and crabs. Consumption of seafood containing palytoxins have caused human illness and death in a number of cases. In addition, humans may be exposed following inhalation of aerosolized palytoxins associated with algal blooms. Specifically, acute exposure to palytoxins are associated with neuromuscular effects including ascending paralysis and muscle damage. (Munday R. Palytoxin toxicology: Animal studies 2011 Toxicon 57:470-477)

**Tuesday, January 29, 2013****Question:**

What was Zyklon B?

**Answer:**

Zyklon B was used as a killing agent by the Nazis operating death camps during World War II. Zyklon B consisted of liquid HCN adsorbed onto a carrier -- "wood fiber disks, dia gravel, or small blue cubes". The cited reference notes "A "typical" can of Zyklon contained 200 grams of HCN adsorbed onto the carrier, and was stored in metal tins marked with a death's head and warning that read: "Giftgas!" (Deathly poisonous gas!)". (Harmon B. TECHNICAL ASPECTS OF THE HOLOCAUST: Cyanide, Zyklon-B, and Mass Murder. Available at <http://nizkor.org/ftp.cgi/camps/auschwitz/cyanide/cyanide.001>)

**Monday, January 28, 2013****Question:**

Only four medications are currently approved by the US FDA for the treatment of alcohol dependence. What are these medications?

**Answer:**

The four medications approved by the FDA to treat alcohol dependence are disulfiram, acamprosate, oral naltrexone, and extended release injectable naltrexone. (Friedmann PD. Alcohol use in adults. 2013 NEJM 368:365-373)

**Friday, January 25, 2013**

**Question:**

White phosphorus is a potentially dangerous material often found as a munition, as a component of fireworks, and may also be found in some insecticides, fertilizers and rodenticides. What physico-chemical characteristic of this chemical is primarily related to its ability to cause injury?

**Answer:**

The characteristic of most concern is the auto-ignition temperature for this chemical. That is the temperature at which combustion takes place without any ignition source. The auto-ignition temperature for white phosphorus is 86 degrees F. Above this temperature, white phosphorus can be expected to ignite spontaneously on contact with air forming phosphorus pentoxide. The cited reference notes that "In wounds, particles of white phosphorus continue to oxidize until debrided, neutralized or consumed, producing a yellow flame with white smoke." (Barillo DJ, et al. Treatment of white phosphorus and other chemical burn injuries at one burn center over a 51-year period. 2004 Burns 30:448-452)

**Thursday, January 24, 2013**

**Question:**

What are probiotics? What are the adverse effects that have been associated with probiotics?

**Answer:**

The cited reference defines probiotics as "live, nonpathogenic microorganisms (usually bacteria or yeasts) marketed as dietary supplements." With regard to adverse effects, probiotics are noted to cause gastrointestinal gas with bloating as well as diarrhea and hiccups. In immunosuppressed individuals probiotics have been associated with the development of serious disease with *Lactobacillus casei* associated with sepsis and *Lactobacillus GG* associated with the development of hepatic abscess. Interestingly, no probiotics have yet been approved by the US Food and Drug Administration for any medical indication. (The Medical Letter, January 7, 2013; 55(1407): 3-4)

**Wednesday, January 23, 2013**

**Question:**

What are the common symptoms associated with the neonatal abstinence syndrome (NAS)?

**Answer:**

The cited reference notes that the "common symptoms of NAS in order of frequency includes tremor, high-pitched cry, sneezing, increased muscle tone, regurgitation and vomiting, poor sleep, loose stools, sweating, excoriation, mottling, nasal stuffiness, low-grade fever, and tachypnea. Impaired weight gain and seizures are seen with untreated NAS." The authors also point out "NAS symptoms severe enough to require pharmacologic treatment occur in 55% to 94% of infants born to opioid-dependent mothers". (Kraft WK and van den Anker J. Pharmacologic management of the opioid neonatal abstinence syndrome. 2012 *Pediatr Clinics of North Am* 59(5): 1147-1165)

**Tuesday, January 22, 2013**

**Question:**

What is the chemical chloropicrin (military designation: PS) used for?

**Answer:**

Chloropicrin (PS) is an irritant with characteristics of a tear gas. It has also found use in agriculture as a soil fumigant. It has also been used as a chemical warfare agent and a riot control agent. It was used in large quantities during World War I and was stockpiled during World War II. However, it is no longer authorized for military use. Chloropicrin has an intensely irritating odor and inhalation of as little as 1 ppm may cause eye irritation and may provide warning of the potential for exposure. ([http://www.cdc.gov/NIOSH/ersbdb/EmergencyResponseCard\\_29750034.html](http://www.cdc.gov/NIOSH/ersbdb/EmergencyResponseCard_29750034.html))

**Monday, January 21, 2013**

**Question:**

What potentially dangerous chemical may be released from the antidote Prussian Blue?

**Answer:**

Prussian Blue is ferric-hexacyanoferrate and may be used to treat internal contamination with isotopes of thallium and cesium. Prussian Blue may release very small amounts of cyanide, generally well below minimal lethal levels. (Yang Y et al. Quantitative measurement of cyanide released from Prussian Blue. 2007 *Clin Tox* 45(7):776-781)

**Friday, January 18, 2013**

**Question:**

Metronidazole is a synthetic 5-nitroimidazole with antiprotozoal and antibacterial activity. What are the adverse neurological effects that have been reported to be associated with the use of this drug?

**Answer:**

The adverse neurological effects that have been reported to be associated with the use of metronidazole include cerebellar disease, encephalopathy, seizures, and peripheral neuropathy. (Kim DW et al. Metronidazole-induced encephalopathy. 2004 *J Neurol Sci* 224:107-111)

**Thursday, January 17, 2013**

**Question:**

What is the classic clinical syndrome associated with INH toxicity?

**Answer:**

According to the cited reference, the classic clinical syndrome associated with INH toxicity includes "seizures, metabolic acidosis, and, in severe cases, respiratory depression and coma". (Minns AB et al. Isoniazid-induced status epilepticus in a pediatric patient after inadequate pyridoxine therapy. 2010 *Pediatr Emer Care* 26:380-381)

**Wednesday, January 16, 2013**

**Question:**

What are the nine isotopes considered to be potential toxicants that may be used in RDDs (radiological dispersion devices)?

**Answer:**

Americium-241; Californium-252; Cesium-137; Cobalt-60; Iridium-192; Plutonium-238; Polonium-210; Radium-226 and Strontium-90 are the isotopes considered to be potential toxicants in RDDs (<http://www.remm.nlm.gov/rdd.htm#isotopes>)

**Tuesday, January 15, 2013****Question:**

Acute baclofen withdrawal, with consequent muscle spasticity, secondary to intrathecal baclofen pump failure or acute infection is not an uncommon occurrence. The administration of benzodiazepines forms the mainstay of acute treatment in this setting. What is the role of oral baclofen in the treatment of acute intrathecal baclofen withdrawal?

**Answer:**

The cited reference notes "Oral baclofen does not achieve concentrations remotely near the range resulting from directly infused ITB and, as a consequence, is not particularly effective for acute baclofen withdrawal." Recommended adjuncts to benzodiazepine administration in this setting include cyproheptadine for serotonergic effects, dantrolene for excessive spasticity and tizanidine for patients with elevated blood pressure in conjunction with spasticity. (Ross JC et al. Acute intrathecal baclofen withdrawal: A brief review of treatment options. 2011 Neurocrit Care 14:103-108)

**Monday, January 14, 2013****Question:**

What is the mechanism of action for strychnine and what are the clinical findings that are classically described for strychnine poisoning?

**Answer:**

The cited reference notes "Strychnine competitively blocks the neuroinhibitory transmitter glycine at postsynaptic sites, especially in the spinal cord. This results in hyperexcitability and convulsions. These convulsions typically involve flexor spasm of the upper limbs, extensor spasm of the lower limbs, opisthotonos, and spasms of the jaw muscles (risus sardonicus)." Patients typically do not lose consciousness but rather tend to be "hyper-alert" with even minimal stimulation triggering spasms. (Meatherall R et al. Toxicokinetics of acute strychnine poisoning. 1997 J Tox Clin Tox 35(6): 617 and O'Callaghan WG, et al. Unusual strychnine poisoning and its treatment: Report of eight cases. 1982 Br Med J Clin Res Ed 285:478)

**Friday, January 11, 2013****Question:**

What clinical laboratory findings raise serious concerns regarding the development of potentially life threatening blood levels of methotrexate (and consequent toxicity) in patients being treated with this drug?

**Answer:**

Pancytopenia as well as laboratory indicators of renal failure should raise serious concerns regarding the continued use of methotrexate. Under these circumstances, clinicians should immediately discontinue the use of the drug and should also consider early treatment with folinic acid. (Strang A and Pullar T. Methotrexate toxicity induced by acute renal failure. 2004 J R Soc Med 97:536-537)

**Thursday, January 10, 2013****Question:**

Certain forms of chemotherapy may result in the development of delayed transient leukoencephalopathy mimicking cerebrovascular accident. Which chemotherapeutics have been associated with this phenomenon?

**Answer:**

The chemotherapeutics that have been associated with the development of delayed transient leukoencephalopathy mimicking cerebrovascular accident include methotrexate, 5-FU, carmofur (a 5-FU derivative), and capecitabine. This phenomenon reportedly occurs in fewer than 2% of patients treated with methotrexate. It has been reported following both intrathecal and high dose intravenous therapy. The clinical course for this phenomenon reportedly mimics a cerebrovascular accident initially with fluctuating symptoms over the course of several days. Symptoms are reversible and generally resolve without residual clinical deficits. (Baehring JM and Fulbright RK. Delayed leukoencephalopathy with stroke-like presentation in chemotherapy recipients. 2008 J Neurol Neurosurg Psychiatry 79:535-539)

**Wednesday, January 9, 2013****Question:**

What is the most common genetic variation relevant to pharmacogenomics?

**Answer:**

SNP's or single-nucleotide polymorphisms are the most common genetic variations relevant to pharmacogenomics. A SNP involves the change of a single nucleotide within the genome. (Wells QS et al. Genetic determinant of response to cardiovascular drugs. 2012 Curr Opin Cardiol 27:253-261)

**Tuesday, January 8, 2013****Question:**

Paclitaxel is an antineoplastic agent often used in the treatment of solid tumors. This agent may be associated with the development of a variety of adverse skin complications. What are the most common adverse dermal effects related to the administration of paclitaxel?

**Answer:**

The most commonly reported skin issues associated with paclitaxel involve local extravasation of drug during intravenous therapy. This can result in local effects ranging from superficial venous thrombosis to painful cellulitis and local skin necrosis. In fact, there is at least one report of full thickness skin necrosis at anatomic sites removed from the site of injection of the drug. (Aboolian A et al. Skin necrosis in the presence of paclitaxel and fluorometholone. 1999 Support Care Cancer 7:158-159)

**Monday, January 7, 2013**

**Question:**

Dan Shen is a Chinese herbal from the root of the plant *Salvia miltiorrhiza*. What laboratory assay might be interfered with for patients taking this widely available Chinese herbal medication?

**Answer:**

Dan Shen contains diterpene quinones known as tanshinones. These are structurally similar to digoxin and under some circumstances may confound serum digoxin levels. The quinones found in Dan Shen are highly protein bound so measuring free digoxin levels would, in most cases, eliminate this problem. (Dasgupta A. Endogenous and exogenous digoxin-like immunoreactive substances. 2002 Am J Clin Path 118:132-140)

**Friday, January 4, 2013**

**Question:**

What is the OSHA "action level" for lead? What is the OSHA requirement for the temporary removal of employees from lead exposure?

**Answer:**

The OSHA action level means "employee exposure, without regard to the use of respirators, to an airborne concentration of lead of 30 micrograms per cubic meter of air (30 ug/m<sup>3</sup>) averaged over an 8-hour period".

OSHA requires the removal of covered employees from lead exposure as follows:

"The employer shall remove an employee from work having an exposure to lead at or above the action level on each occasion that a periodic and a follow-up blood sampling test conducted pursuant to this section indicate that the employee's blood lead level is at or above 60 micrograms/100 g of whole blood; and,

The employer shall remove an employee from work having an exposure to lead at or above the action level on each occasion that the average of the last three blood sampling tests conducted pursuant to this section (or the average of all blood sampling tests conducted over the previous six (6) months, whichever is longer) indicates that the employee's blood lead level is at or above 50 micrograms/100 g of whole blood; provided, however, that an employee need not be removed if the last blood sampling test indicates a blood lead level below 40 micrograms/100 g of whole blood." (OSHA (1910.1025(k)(1)(i) (A) and (B)- [http://www.osha.gov/pls/oshaweb/owadisp.show\\_document?p\\_table=standards&p\\_id=10030](http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standards&p_id=10030))

**Thursday, January 3, 2013**

**Question:**

How many phases for clinical trials does the FDA define? What are the differences between phase 3 clinical trials and phase 4 clinical trials?

**Answer:**

The FDA describes five (5) phases for clinical trials numbered 0,1,2,3,4. Phase 3 studies are designed to gather information about safety and effectiveness by studying different populations and different dosages and by using the drug in combination with other drugs. These are pre-marketing studies. Phase 4 studies occur after FDA has approved a drug for marketing and include . These post market requirement and commitment studies that are required of or agreed to by the study sponsor.

(<http://clinicaltrials.gov/ct2/about-studies/learn#ClinicalTrials>)

**Wednesday, January 2, 2013**

**Question:**

What is the cause for the renal injury associated with ethylene glycol poisoning?

**Answer:**

As ethylene glycol is metabolized, oxalic acid is formed. Calcium oxalate forms when this oxalic acid combines with ionized calcium. This calcium oxalate precipitates within the renal tubules and is thus posited to be the cause for ethylene glycol induced kidney damage. (Brent J. Fomepizole for ethylene glycol and methanol poisoning. 2009 NEJM 360(21): 2216-2222)

**Tuesday, January 1, 2013**

**Question:**

What is the mechanism of action of the rodenticide bromethalin?

**Answer:**

Bromethalin is a neurotoxic substance found in a variety of rodenticides. The cited reference notes the "presumed mechanism of action of bromethalin is uncoupling of oxidative phosphorylation resulting in depletion of cellular adenosine triphosphate (ATP). Decreased ATP production disrupts the function of the sodium-potassium ion channel pumps leading to cerebral edema and elevated CSF pressure". (Pasquale-Styles MA et al. Fatal bromethalin poisoning. 2006 J Forensic Sci 51(5):1154-1157)

**Monday, December 31, 2012**

**Question:**

What are refractory ceramic fibers (RCFs)? What are the biopersistence issues for humans exposed to RCFs?

**Answer:**

Refractory ceramic fibers (RCFs) are synthetic vitreous fibers with high tensile strength, flexibility and excellent thermal resistance. They find use where high temperature insulation is necessary such as in furnaces and for automotive and aerospace applications. RCFs are produced by melting kaolin clay or silica/alumina solutions either as sole constituents or combined with small amounts of various metal oxides. The cited reference points out that the production process for RCFs can result in the generation of RCFs of respirable size. The cited reference also reports RCFs "can persist in human lung tissue for up to 20 years and may contribute to the significant association between cumulative fiber exposure and radiographic pleural changes". (Lockey JE et al. Biopersistence of refractory ceramic fiber in human lung tissue and a 20-year follow-up of radiographic pleural changes in workers. 2012 J Occ Env Med 54(7):781-788)

**Friday, December 28, 2012**

**Question:**

What is the antidote for ricin poisoning and what is the role for hemodialysis in the treatment of ricin casualties?

**Answer:**

No antidote against ricin toxicity is currently available. Ricin is not amenable to removal by hemodialysis. Treatment for ricin related toxicity essentially involves supportive care. (Audi J et al. Ricin poisoning- A comprehensive review. 2005 JAMA 294(18):2342-2351)

**Thursday, December 27, 2012**

**Question:**

Brodifacoum is a long-acting anticoagulant rodenticide. What is the duration of action of this compound?

**Answer:**

The duration of action of brodifacoum reportedly ranges from 51 days to 9 months in the setting of overdose. (Caravati EM et al. Long-acting anticoagulant rodenticide poisoning: An evidence-based consensus guideline for out-of-hospital management. 2007 Clin Tox 45 (1): 1-22)

**Wednesday, December 26, 2012**

**Question:**

Buprenorphine is used for the treatment of opioid dependence. This medication manifests an effect unique among opioid drugs known as a “ceiling effect”. What is the “ceiling effect” with regard to buprenorphine?

**Answer:**

Buprenorphine produces euphoria and respiratory depression in a dose dependent manner (similar to other opioids). However, with buprenorphine, these effects increase until, at moderate doses, the effects reach a plateau and no longer continue to increase. This “ceiling effect” tends to make respiratory depression due to buprenorphine less likely in a habituated opioid user. It is important to note, however, that respiratory depression may occur in opioid naive patients (especially children) before this ceiling level is attained. (CDC MMWR 61(49): 997-1000)

**Tuesday, December 25, 2012**

**Question:**

What are the most common clinical findings associated with valproic acid-related hepatotoxicity? What are the risk factors for the development of valproic acid-related hepatotoxicity?

**Answer:**

The most common clinical findings associated with valproic acid-related hepatotoxicity are fatigue, lethargy, jaundice, nausea, vomiting, worsening seizures and anorexia. The cited reference notes the risk factors for the development of severe valproic acid-related hepatotoxicity include young age (especially younger than 2 years of age), developmental delay, congenital metabolic disorders (e.g. mitochondrial enzyme deficiencies), pre-existing liver disease, severe epilepsy treated with multiple drugs, ketogenic diets, severe physiological stress such as serious infection. (Lheureux P and Hantson P. Carnitine in the treatment of valproic acid-induced toxicity. 2009 Clin Tox 47(2): 101-111)

**Monday, December 24, 2012**

**Question:**

A patient diagnosed with infectious mononucleosis has developed a diffuse morbilliform (maculopapular) rash on the trunk and back. What drug has this patient likely been recently treated with?

**Answer:**

As many as 95% of patients with infectious mononucleosis who receive ampicillin or amoxicillin will develop morbilliform rashes. The cited reference also notes that other beta lactam antibiotics may also result in the development of similar rashes but only in roughly 40 to 60% of cases. (Luzuriaga K and Sullivan JL. Infectious mononucleosis. 2010 NEJM 362:1993-2000)

**Friday, December 21, 2012**

**Question:**

Which enzymes are involved in the metabolism of methadone and which metabolites result from methadone metabolism?

**Answer:**

According to the cited reference, methadone is metabolized by cytochrome P450 enzymes 1A2, 2B6, 2C9, 2C19, 2D6, and 3A4 to EDDP (2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine) and EMDP (2-ethyl-5-methyl-3,3-diphenyl-1-pyrrolidine). (Letsky MC et al Cause of death conundrum with methadone use. 2011 Am J Forensic Med Pathol 32:193-196)

**Thursday, December 20, 2012**

**Question:**

What is Freon?

**Answer:**

Freon is actually a trade name for a set of halogenated hydrocarbon products. These products have been widely used in refrigeration and air conditioning units. The “freons” are odorless, colorless and highly lipid soluble compounds that are rapidly absorbed following inhalation. The abuse of these products by “tapping in” to above ground air conditioning units has been noted in the literature and has resulted in deaths. Over the past decade, the industry has been replacing Freon containing air conditioning units with alternative refrigerants over the past decade. (Caplan JP et al. Air conditioner refrigerant inhalation: A habit with chilling consequences. 2012 Psychosomatics 53:273-276)

**Wednesday, December 19, 2012**



**Question:**

Which nickel compound is the most dangerous with regard to acute exposure? Which route of exposure is most concerning with regard to this compound?

**Answer:**

Nickel carbonyl is the most potentially harmful nickel compound if inhaled on an acute basis. If nickel carbonyl is inhaled, it is absorbed very rapidly and distributed to a variety of solid organs in the body. In severe cases, acute nickel carbonyl exposure has been reported to cause death. (Raymond CS et al. Inhalational nickel carbonyl poisoning in waster processing workers. 2005 Chest 128(1))

**Tuesday, December 18, 2012**

**Question:**

Which drug is most commonly implicated in deaths that occur in hot tubs or saunas?

**Answer:**

The primary drug that contributes to deaths in hot tubs or saunas is ethanol with cocaine and cocaine-ethanol in combination as the second most common drug related contributors to these deaths. (Press E. The health hazards of saunas and spas and how to minimize them. 1991 Am J Pub Health 81:1034-1037)

**Monday, December 17, 2012**

**Question:**

A recent report implicated the substance DMAA as a contributing cause of death in several active duty military personnel. What is DMAA?

**Answer:**

DMAA, 1,3 dimethylamylamine, is also known as methylhexanamine. This chemical is a sympathomimetic agent that first found its way into the market place in 1948 as a decongestant. It was removed from the market in 1983 but has since been re-marketed in "geranium oil" or "geranium extract" as well as other dietary supplements. DMAA has recently been implicated in exertion and heat related deaths in soldiers. (Eliason MJ et al. Case reports: Death of active duty soldiers following ingestion of dietary supplements containing 1,3 dimethylamylamine (DMAA) 2012 Mil Med 12:1455-1459)

**Friday, December 14, 2012**

**Question:**

What is the so-called "narcotic bowel syndrome"?

**Answer:**

The cited reference describes narcotic bowel syndrome (NBS) as "chronic or recurrent abdominal pain associated with escalating doses of narcotics". NBS may be most frequently manifest when the analgesic effects of chronically administered narcotics are decreasing and may include nausea and vomiting as well as distention and constipation. Interestingly, in some cases, NBS symptoms may be worse following the ingestion of food and this may cause some patients to avoid eating with consequent weight loss. (Grover CA et al. Narcotic Bowel Syndrome. 2012 J Emerg Med 43(6):992-995)

**Thursday, December 13, 2012**

**Question:**

The compound ethyl glucuronide has been proposed as a biomarker for the ingestion of what substance? What substrates have been proposed to test for this compound?

**Answer:**

Ethyl glucuronide has been proposed as a biomarker for the ingestion of ethanol. It has been suggested that this marker be applied to urine, serum and/or hair testing. However, as the author for the cited article notes: "challenges associated with factors such as establishing appropriate cut-off levels capable of distinguishing between drinking and non-beverage sources of ethanol exposure, non-uniform laboratory reporting limits, sample stability, and microbial activity substantially complicate accurate interpretation of results." (Palmer RB A review of the use of ethyl glucuronide as a marker for ethanol consumption in forensic and clinical medicine. 2009 Seminars Diag Path 26:18-27)

**Wednesday, December 12, 2012**

**Question:**

In 1965, Sir Austin Bradford Hill famously addressed the question of determining association versus the determination of causation with regard to the environmental and disease. What are the elements (or viewpoints as he termed them) that Bradford Hill listed as being important in this exercise? In 1965, Sir Austin Bradford Hill famously addressed the question of determining association versus the determination of causation with regard to the environmental and disease. What are the elements (or viewpoints as he termed them) that Bradford Hill listed as being important in this exercise?

**Answer:**

The elements addressed by Bradford-Hill in his famous discussion of association and causation were (in the order he listed them): 1- Strength, 2- Consistency, 3- Specificity, 4-Temporality, 5- Biological gradient, 6- Plausibility, 7- Coherence, 8-Experiment and 9- Analogy. Importantly, Bradford-Hill stated "None of my nine viewpoints can bring indisputable evidence for or against the cause and effect hypothesis and none can be required as a sine qua non. What they can do, with greater or less strength, is to help us make up our minds on the fundamental question-is there any other way of explaining the set of facts before us, is there any other answer equally, or more, likely than cause and effect?" (Hill AB. The environment and disease: Association or causation? 1965 Proc Royal Soc Med 58(5): 295-300)

**Tuesday, December 11, 2012**

**Question:**

In 2009, the acne medication Accutane (isotretinoin) was removed from the market by it's manufacturer. Lay press articles have identified that one of the reasons the manufacturer opted for removal from the market was a purported association between the use of isotretinoin and the development of what disorder?

**Answer:**

One of the reasons Accutane was removed from the market was the purported association between its use and the development of inflammatory bowel disease (IBD). However, a recently reported, extensive, 12 year study, showed no significant association between IBD and isotretinoin use. (Alhusayen RO, Juurlink DN et al. Isotretinoin use and the risk of inflammatory bowel disease: A Population-Based Cohort Study. 2012 J Invest Dermatol (epub ahead of print)

**Monday, December 10, 2012**

**Question:**

Rivastigmine is a cholinesterase inhibitor sometimes used in the treatment of dementia. This drug is often used as a transdermal patch however the delivery of this drug transdermally can be associated with significant cutaneous reactions. How can one differentiate irritant reactions to rivastigmine transdermal from true allergic reactions to the drug?

**Answer:**

Most reactions to rivastigmine-containing transdermal patches are of an irritant type. The cited reference notes that these reactions are “diagnosed clinically by the presence of a pruritic, erythematous, eczematous plaque strictly confined to the borders of the patch”. According to the cited source, an allergic reaction due to a transdermal patch “can be differentiated by the presence of vesicles and/or edema and erythema beyond the boundaries of the transdermal patch and lack of improvement of the lesion 48 hours after removal of the offending treatment”. (Greenspoon J et al. Transdermal rivastigmine- Management of cutaneous adverse events and review of the literature. 2011 CNS Drugs 25(7):575-583)

**Friday, December 7, 2012**

**Question:**

What are the most common adverse effects reported during clinical trials of electronic cigarettes also known as “e-cigarettes”?

**Answer:**

Non-productive cough, dry mouth and sore throat are the most common adverse effects reported. (Electronic cigarettes for smoking cessation. 2012 The Medical Letter 54(1404):93-94)

**Thursday, December 6, 2012**

**Question:**

People who consume game meat harvested from animals killed using lead ammunition typically are able to avoid ingesting lead shot or bullets retained in the meat. Nonetheless, eating such game meat may indeed pose a risk for the development of elevated lead levels. How is this possible?

**Answer:**

Recent work suggests that lead bullets and lead shot can be extensively fragmented on impact and thus leave residual tiny particles of lead dispersed in the soft tissue of the killed game. These tiny lead particles may not be easily discerned by the person eating the cooked game meat. The cited paper concluded “the potential health hazard from lead ingested in the meat of game animals may be larger than previous risk assessments indicate, especially for vulnerable groups, such as children, and those consuming large amounts of game.” (Pain DJ et al. Potential hazard to human health from exposure to fragments of lead bullets and shot in the tissues of game animals. 2010 PLOS ONE 5(4):1-17)

**Wednesday, December 5, 2012**

**Question:**

What is the most common cause for acute gastroenteritis (in adults) resulting in a visit to a hospital emergency department in the United States today?

**Answer:**

The most common cause for acute gastroenteritis (in adults) resulting in a visit to a hospital emergency department in the United States today is infection with noroviruses. (Bok K and Green KY. Norovirus gastroenteritis in immunocompromised patients. 2012 NEJM 367:2126-2132)

**Tuesday, December 4, 2012**

**Question:**

How effective is hemodialysis in removing the drug dabigatran?

**Answer:**

The manufacturers of dabigatran studied hemodialysis for drug removal in hemodialysis dependent patients and reported that 61% and 68% of the drug was removed at 2 hours and 4 hours respectively. (Stangier J et al. Influence of renal impairment on the pharmacokinetics and pharmacodynamics of oral dabigatran etexilate: an open label, parallel-group, single centre study. 2010 Clin Pharmacokinet 49:259-268 as cited in Chen BC et al. Hemorrhagic complications associated with dabigatran use. 2012 Clin Tox 50(9):854-857)

**Monday, December 3, 2012**

**Question:**

What is the recommended dosing for octreotide when used for the treatment of sulfonylurea poisoning?

**Answer:**

The review cited below made the following recommendations based on published clinical and pharmacokinetic data: for children, give octreotide 1-1.5 micrograms/Kg IV or SC followed by 2-3 more doses 6 hours apart; for adults, give octreotide 50 micrograms IV or SC followed by three 50 microgram doses every 6 hours. (Glatstein M et al. Octreotide for the treatment of sulfonylurea poisoning. 2012 Clin Tox 50(9):795-804)

**Friday, November 30, 2012**

**Question:**

The use of naloxone has been advocated by some as a treatment adjunct for patients suffering hepatic encephalopathy. What is the rationale for the use of naloxone in this setting?

**Answer:**

Some endogenous opioid peptides are reported to be elevated in individuals suffering from liver disease (both chronic and acute). It is theorized that these opioid peptides, when concentrated in the central nervous system, may be responsible for some aspects of hepatic encephalopathy. (Jiang Q, et al. Naloxone in the management of hepatic encephalopathy. 2010 J Clin Pharm Ther 35:333-341)

**Thursday, November 29, 2012**

**Question:**

So-called “compounding pharmacies” are establishments that essentially make and sell their own formulations of a variety of medications. Recently compounding pharmacies have come under scrutiny resulting from an outbreak of fungal meningitis traced to a specific compounding pharmacy. How does the regulation of compounding pharmacies differ from traditional drug manufacturers?

**Answer:**

According to the cited reference, “Traditional compounding pharmacies are not registered with the FDA as drug manufacturers, the agency doesn’t approve their prescriptions before marketing, and related adverse events need not be reported to the FDA. State law generally controls recordkeeping, certifications, and licensing for compounding pharmacies.” Compounding pharmacies are specifically “not subject to federal recordkeeping and reporting rules for drug manufacturers”. (Outterson K. Regulating compounding pharmacies after NECC. 2012 NEJM 367:1969-1972)

**Wednesday, November 28, 2012**

**Question:**

Exposure to what chemical has been posited by some to be responsible for a bronchiolitis obliterans syndrome known as “popcorn workers lung”?

**Answer:**

It has been theorized that some workers who may have been exposed to the chemical diacetyl may have developed a bronchiolitis obliterans syndrome that has come to be known as “popcorn workers lung”. (Van Rooy F, et al. Bronchiolitis obliterans syndrome in chemical workers producing diacetyl for food flavorings. 2007 Am J Resp Crit Care Med 176:498-504)

**Tuesday, November 27, 2012**

**Question:**

“Methadone mouth” is a condition characterized by very poor oral hygiene with rapid tooth destruction seen in many individuals on methadone maintenance therapy. What is the difference between “meth mouth” and “methadone mouth”?

**Answer:**

While both oral conditions are similar, “meth mouth” is associated with the long-term use of methamphetamine and tends to be associated with greater degrees and amounts of tooth decay when compared with methadone mouth. Methadone users however tend to have a higher overall prevalence of oral disease including teeth, gum, jaw, and temporo-mandibular joint disease. While the reasons for this difference are unclear, the cited article notes that co-morbid clinical depression in methadone patients may contribute to greater apathy towards oral hygiene and general dental care. (Brandani M. Methadone and oral health- A brief review. J Dental Hygiene 85(2): 92-98)

**Monday, November 26, 2012**

**Question:**

Opium use has been shown to be associated with the development of which cancers in humans?

**Answer:**

The human cancers that have been reported to be associated with opium use include esophageal squamous cell carcinoma, laryngeal carcinoma and bladder cancer. While the specific mechanisms at play for this phenomenon are yet to be proven it is likely that the negative effects of opium on the human immune system plays a role. In addition, the compound diethylnitrosamine (DEN) is produced by the pyrolysis of opium. DEN is a strong mutagen that promotes the alkylation of DNA and thus may influence the induction of cancer. (Hosseini SY et al. Opium consumption and risk of bladder cancer: A case-control analysis. 2010 Urologic Onc 28:610-616)

**Friday, November 23, 2012**

**Question:**

What are the risk factors for SILENT (Syndrome of Irreversible Lithium-Effectuated Neurotoxicity)?

**Answer:**

The risk factors for SILENT include: age (mean age 48 years of age), gender (female prevalence), dose (wide range but can occur even at therapeutic doses), psychiatric diagnoses (more prevalent in patients with marked psychotic symptoms), neurologic status (seizure prone patients may be at greater risk), and misc. factors (infection, dehydration, poor renal function. (Adityanjee et al. The syndrome of irreversible lithium-effectuated neurotoxicity. 2005 Clin Neuropsychopharmacol 28(1):38-49)

**Thursday, November 22, 2012**

**Question:**

What potentially harmful chemicals might tannery workers be exposed to?

**Answer:**

Tannery workers (especially in emerging countries where regulatory controls may be sub standard) may be exposed to azo-colorants, chromium, formaldehyde, pentachlorophenol, sodium sulfide and sulfuric acid. (Tremblay J. Bangladesh’s leather horror. Chemical & Engineering News, November 19,2012, p 26)

**Wednesday, November 21, 2012**

**Question:**

What is flock workers lung?

**Answer:**

Flocking is an industrial process involving the application of very short lengths of synthetic fibers to backing material in order to produce “plush” or “velvet-like” textiles. Flock workers lung is an interstitial lung disorder first identified and reported in the late 1990s in workers in the portion of the textile industry that manufactures plush type fabrics. The specific etiology of flock workers lung has not been fully defined but the cited reference notes “injury pattern and environmental studies suggest a chronic immunologic response to inhaled material”. (Boag A, et al. The pathology of interstitial lung disease in nylon flock workers. 1999 Am J Surg Path 23(12):1539)

**Tuesday, November 20, 2012**

**Question:**

Clenbuterol toxicity has occurred secondary to its use as a heroin adulterant and due to its intentional overuse in bodybuilders. What other source for clenbuterol toxicity has been reported?

**Answer:**

Clenbuterol toxicity has been reported from ingesting the meat of clenbuterol treated animals. (Manini A et al. A novel neuromuscular syndrome associated with clenbuterol-tainted heroin. 2008 Clin Tox 46:1088-1092)

**Monday, November 19, 2012****Question:**

Exposure to chlorine gas can be a serious inhalational threat in a variety of settings. Such exposures are capable of causing acute injury to the lungs and respiratory tree but recent research has focused on the potential for chlorine gas exposure to influence vascular injury in a variety of extra-pulmonary tissues. What is the likely mechanism for this somewhat underappreciated potential adverse effect related to the inhalation of chlorine gas?

**Answer:**

While the specific mechanisms related to extra- pulmonary effects of inhaled chemicals are still being studied, one probable mechanism with regard to chlorine gas involves the development of dysfunction of the endothelial nitric acid (NO) signaling pathway. This may lead to widespread endothelial dysfunction and is thought to play a role in the development of systemic inflammatory vascular disease. The cited reference notes "In general this occurs by either decreased NO synthesis and/or redirection of NO from "physiologic" to "pathologic"(or proinflammatory) signaling processes. (Samal A et al. Potential for chlorine gas-induced injury in the extrapulmonary vasculature. 2010 Proc Am Thorac Soc 7:290-293)

**Friday, November 16, 2012****Question:**

What are the delayed type hypersensitivity reactions recognized in association with antiepileptic drugs?

**Answer:**

These reactions, known as "severe cutaneous adverse drug reactions" or "SCARS" include toxic epidermal necrolysis (TEN), Stevens Johnson Syndrome, and DRESS (drug rash with eosinophilia and systemic symptoms). (Yang CY et al. Severe cutaneous adverse reactions to antiepileptic drugs in Asians. 2011 Neurology 77:2025-2033)

**Thursday, November 15, 2012****Question:**

What is the IDLH (Immediately Dangerous To Life or Health concentration) for carbon monoxide?

**Answer:**

The IDLH (Immediately Dangerous To Life or Health concentrations) for carbon monoxide is 1200 parts per million. This level is based on acute inhalation toxicity data in humans. (Henderson Y, et al [1921]. Physiological effects of automobile exhaust gas and standards of ventilation for brief exposures. J Ind Hyg III(3):79-92; NIOSH [1972]; NIOSH criteria for a recommended standard: occupational exposure to carbon monoxide. Cincinnati, OH: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. HSM 73-11000, and Stewart RL and Peterson MR [1970]. Experimental human exposure to carbon monoxide. Arch Environ Health 12:154-164)

**Wednesday, November 14, 2012****Question:**

What are the five main Phase II reactions?

**Answer:**

The five main Phase II reactions are: glucuronidation, acetylation, glutathione conjugation, sulfation and methylation. (O'Donnell JJ et al. Clinical pharmacology for the primary care physician. 2012 Disease-a-Month 58(10): 553-612)

**Tuesday, November 13, 2012****Question:**

Which drug, used in the treatment of bipolar disorder, has been used in the treatment of neutropenia?

**Answer:**

Lithium is known to cause leukocytosis with an increase in neutrophil forms of white blood cells. The clinical utility for the use of lithium in this application remains controversial and proof of clinical efficacy has yet to be demonstrated. The use of colony stimulating factors has essentially made the question a moot point. (Boggs D. The hematopoietic effects of lithium. 1983 Semin Hematol 20:129-138)

**Monday, November 12, 2012****Question:**

What is the prevalence of acute kidney injury in patients with acetaminophen-induced hepatotoxicity?

**Answer:**

One study of over 300 patients (liver transplant recipients excluded) reported that renal function remained normal in only 21 % of patients with the remainder developing some degree of acute renal injury. Despite the fact that renal injury is very common in patients with acetaminophen-induced liver toxicity, recovery of renal function over time is the rule with only a small percentage of patients remaining dialysis dependent. (O'Riordan A, et al. Acute kidney injury in patients admitted to a liver intensive therapy unit with paracetamol-induced hepatotoxicity 2011 Nephro Dialysis Transplantation 26(11):3501-3508)

**Friday, November 9, 2012**

**Question:**

What are the clinical manifestations of heroin pyrolysate-induced spongiform leukoencephalopathy that may result from the process of heroin use known as “chasing the dragon”?

**Answer:**

Heroin pyrolysate-induced spongiform leukoencephalopathy is characterized by a spectrum of symptoms ranging from ataxia, akathisia and apathy to the development of tremor, myoclonus, choreoathetoid movements, so-called “stretching spasms”, hypotonic paresis, and hyperpyrexia. (Filley CM and Kleinschmidt-Demasters BK. Toxic leukoencephalopathy. 2001 NEJM 345(6):425-432) as cited in (Long H et al. A fatal case of spongiform leukoencephalopathy linked to “chasing the dragon” 2003 Clin Tox 41(6):887-891)

**Thursday, November 8, 2012****Question:**

What toxicological entity should be considered in patients who appear to be septic when the specific source diagnosis is not immediately apparent?

**Answer:**

Several authors have suggested that patients presenting with a sepsis-like syndrome should be promptly evaluated for salicylate toxicity. (Leatherman JW, Schmitz PG. Fever, hyperdynamic shock, and multiple- system organ failure. A pseudo-sepsis syndrome associated with chronic salicylate intoxication. Chest 1991;100:1391–1396 as cited in Glisson JK et al. Current management of salicylate-induced pulmonary edema)

**Wednesday, November 7, 2012****Question:**

What is Angel's trumpet?

**Answer:**

Angel's trumpet is an ornamental plant originally from South America. It is in the genus Brugmansia. The plant contains a number of parasympatholytic chemicals including hyoscyamine, atropine and scopolamine. Ingestion of parts of this plant may be associated with a severe anticholinergic toxidrome. (Vunda A and Alcoba G. Mydriasis in the garden. 2012 NEJM 367(14):1341.

**Tuesday, November 6, 2012****Question:**

Phosgene reacts with human tissue either via hydrolysis or acylation. Which chemical mechanism is felt to be of the most clinical import following phosgene exposure?

**Answer:**

Acylation is probably the more important reaction and is likely responsible for the lung damage that is characteristic of phosgene exposure. (Grainge C and Rice P. Management of phosgene induced acute lung injury. 2012 Clin Tox 48:497-508)

**Monday, November 5, 2012****Question:**

What percentage of women admit to use of one or more illicit substances during pregnancy?

**Answer:**

In a US survey, more than 6% of women reported polysubstance use (including tobacco, alcohol, and prescription medicines) and 4.7% admitted use of one or more illicit substances during pregnancy. (Havens JR, et al. Factors associated with substance use during pregnancy: results from a national sample. Drug Alcohol Depend 2009; 99:89–95 as cited in Brunet BR et al. Monitoring pregnant woman's illicit opiate and cocaine use with sweat testing. 2010 Ther Drug Monit 32:40-49)

**Friday, November 2, 2012****Question:**

What is formication? The abuse of which drug has been associated with this phenomenon?

**Answer:**

Formication involves delusions where the affected individual believes that they are infested with bugs and that they are being bitten by those bugs. As a result these individuals continuously physically pick at the areas of their skin where they perceive these bugs. 40%-70% (or more) of methamphetamines abusers report formication (“meth mites”). (Rusyniak DE. Neurologic manifestations of chronic methamphetamine abuse. Neurologic Clinics 2011 29:641-655)

**Thursday, November 1, 2012****Question:**

What is the normal QTc for patients age 1 thru 15 years and what is considered to be prolonged in this age group?

**Answer:**

The suggested Bazett-corrected QTc values for QT prolongations for ages 1 through 15 years are as follows. Normal for this age group is considered to be less than 440 milliseconds. Prolongation is considered to begin at 460 milliseconds for this age group. (Goldenberg I et al. QT interval: How to measure it and what is “normal”. 2006 J Cardiovasc Electrophysiol 17:333-336)

**Wednesday, October 31, 2012****Question:**

What are the two known species of venomous lizards inhabiting the US and Mexico?

**Answer:**

The two venomous species of lizard are *Heloderma suspectum* (Gila monster) and *Heloderma horridum* (beaded lizard). The range for the Gila monster includes southwestern Utah, southern Nevada, and San Bernardino County, California, Arizona and southwestern New Mexico. It ranges south into Mexico through Sonora to northwestern Sinaloa while the beaded lizard is found essentially exclusively in Mexico. (Heffelfinger RN et al. Lizard bites of the head and neck. 2012 J Emerg Med 43(4): 627-629)

**Tuesday, October 30, 2012**

**Question:**

Tilmicosin (Micotil ®) is a macrolide antibiotic used by veterinarians in the prevention and/or treatment of respiratory infections in bovines. The study cited below reported almost 1300 cases of human exposure to this drug over a five-year period. What are the clinical effects following the injection of this drug in humans, what is the likely mechanism of toxicity in humans for this drug, and what drugs are recommended as contraindicated in the treatment of the adverse effects of tilmicosin?

**Answer:**

The signs and symptoms reported after the injection of tilmicosin in humans include tachycardia, hypotension, pulmonary edema, respiratory failure, chest tightness, cardiomegaly, agitation and erythema at the site of injection. The likely mechanism of toxicity for tilmicosin is calcium channel blockade. Based on limited studies in swine, the manufacturer recommends against the use of either beta adrenergic antagonists or epinephrine in the treatment of humans who have been exposed to tilmicosin. (Oakes J and Seifert S. American Association of Poison Control Centers Database Characterization of Human Tilmicosin Exposures, 2001–2005. 2008 J Med Tox 4(4): 225-231 and Black Box Warning from Elanco Animal Health issued October 17, 2012)

**Monday, October 29, 2012**

**Question:**

Many people take fish oil supplements either as prescribed by a physician or via health food stores and various online sources. What are the potential adverse effects of these fish oil supplements and what is the effect on prevention of cardiovascular disease?

**Answer:**

The cited reference reports that fish oil supplements are usually well tolerated. However, they may be associated with dyspepsia and a “fishy” aftertaste. In addition, some diabetics taking large doses of these supplements may have poorer glycemic control. Large doses of fish oil have been reported to inhibit platelet aggregation. Finally, recent studies do not provide conclusive evidence that fish oil supplements prevent cardiac or vascular disease. (The Medical Letter October 15, 2012 54(1401):83)

**Friday, October 26, 2012**

**Question:**

What is selenosis and what symptoms are consistent with the diagnosis of selenosis?

**Answer:**

Selenosis is the term sometimes used to describe a constellation of symptoms associated with selenium toxicity. The cited reference points out that selenosis may include alopecia and/or brittleness of the hair as well as nail abnormalities, skin rash, and gastrointestinal symptoms. In addition, garlic breath odor and abnormal levels of mental alertness may be noted. In geographic areas where high soil selenium concentrations occur, alopecia and nail dystrophy are the most commonly reported findings related to selenium. (Aldosary BM et al. Case series of selenium toxicity from a nutritional supplement. 2012 Clin Tox 50:57-64)

**Thursday, October 25, 2012**

**Question:**

Linezolid is an oxazolidinone antibiotic first approved in 2000 for the treatment of gram-positive infections resistant to other drugs. What is the mechanism of action of linezolid and what are the long-term toxicities specifically associated with this drug's mechanism of action?

**Answer:**

Linezolid binds to the 23S ribosomal RNA moiety of the bacterial 50S ribosomal subunit and thus inhibits the synthesis of protein. The cited reference notes that optic neuropathy and a variety of peripheral neuropathies, as well as bone marrow suppression and hyperlactatemia are likely related to the inhibition of mitochondrial protein synthesis. (Lee M et al. Linezolid for treatment of chronic extensively drug-resistant tuberculosis. 2012 NEJM 367:1508-1518)

**Wednesday, October 24, 2012**

**Question:**

Human exposure to laundry detergent “pods” have recently been addressed as possibly representing a special hazard when compared to “non-pod” laundry detergents. What are the most frequently reported signs and symptoms of pod laundry detergent exposure and how do those findings compare with signs and symptoms associated with non-pod detergent exposures?

**Answer:**

The most frequently reported signs and symptoms of laundry detergent exposure include vomiting (pod-exposed: 251, 55%; non-pod-exposed: 139, 34%), coughing or choking (pod-exposed: 70, 15%; non-pod-exposed: 45, 11%), eye irritation or pain (pod-exposed: 51, 11%; non-pod-exposed: 68, 16%), red eyes/conjunctivitis (pod-exposed: 38, 8%; non-pod-exposed: 36, 9%), drowsiness or lethargy (pod-exposed: 34, 7%; non-pod-exposed: nine, 2%), and nausea (pod-exposed: 26, 6%; non-pod-exposed: 18, 4%). Only vomiting ( $p < 0.001$ ), drowsiness ( $p < 0.001$ ), and coughing or choking ( $p = 0.048$ ) were significantly more common with reported exposures to laundry detergent pods when compared with reported exposures to non-pod laundry detergents. Eye irritation or pain was significantly more common in non-pod laundry detergent exposures ( $p = 0.026$ ). No significant association was found for red eyes/conjunctivitis or nausea in the comparison between pod and non-pod laundry detergent exposures ( $p > 0.05$ ). (MMWR. Health hazards associated with laundry detergent pods-United States. October 19, 2012 / 61(41):825-829)

**Tuesday, October 23, 2012**

**Question:**

Rocuronium can be used as an alternative neuromuscular blocking agent (NMBA) to succinylcholine in order to accomplish rapid sequence endotracheal intubation. What reversal agent is indicated if rapid antagonism of rocuronium effects becomes necessary?

**Answer:**

The cited reference points out that “even profound neuromuscular block with rocuronium can be quickly antagonized with sugammadex and goes on to note that “sugammadex, binds the rocuronium molecules in a 1:1 ratio without having an effect on the plasma cholinesterase or on any receptor system in the human body”. (Sorensen MK et al. Rapid sequence induction and intubation (with rocuronium–sugammadex compared with succinylcholine: a randomized trial. 2012 Br J Anaesthesia 108(4): 682-689)

**Monday, October 22, 2012****Question:**

What are MRLs as promulgated by the Agency for Toxic Substances Disease Registry (ATSDR) and what potential health effects are addressed by MRLs?

**Answer:**

The ATSDR MRL, or minimal risk level, is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse non-cancer health effects over a specified duration of exposure. These substance specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors and other responders to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean up or action levels for ATSDR or other Agencies. It is also important to recognize that MRLs address NON-cancer effects only. (<http://www.atsdr.cdc.gov/mrls/index.asp>)

**Friday, October 19, 2012****Question:**

What bio-marker has been used in the occupational setting to help determine workplace exposure to vinyl chloride?

**Answer:**

Urine assays for thiodiglycolic acid (TDG) have been used in the occupational setting to assess for exposure to vinyl chloride. (Toxicological Profile for Vinyl Chloride. US Dept of Health and Human Services; ATSDR. July, 2006: available at: <http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=282&tid=51>)

**Thursday, October 18, 2012****Question:**

Proton pump inhibitors may increase the risk for what specific pulmonary complication?

**Answer:**

A recent meta analysis of eight observational studies showed that the overall risk of pneumonia was slightly higher among people using proton pump inhibitors (adjusted odds ratio [OR] 1.27, 95% confidence interval [CI] 1.11–1.46, 12 90.5%) (Eom C, et al. Use of acid-suppressive drugs and risk of pneumonia: a systematic review and meta-analysis. 2011 CMAJ 183(3):309-319)

**Wednesday, October 17, 2012****Question:**

What is the most common cause of fatal food-induced anaphylaxis in the US?

**Answer:**

Peanuts are the most common cause of fatal food-induced anaphylaxis in the US. (Finkleman FD. Peanut allergy and anaphylaxis. 2010 Curr Opin Immunology 22:783-788)

**Tuesday, October 16, 2012****Question:**

What adverse effects were associated with each of the following weight loss drugs resulting in their removal from the market: aminorex, fenfluramine and dexfenfluramine, phenylpropanolamine, rimonabant, and sibutramine?

**Answer:**

Aminorex- pulmonary hypertension  
Fenfluramine/dexfenfluramine- cardiac valvulopathy  
Phenylpropanolamine-stroke  
Rimonabant- suicidal ideation and behavior  
Sibutramine- myocardial infarction, stroke  
(Coleman E et al. The FDA's assessment of two drugs for chronic weight management. 2012 NEJM online first-  
[http://www.nejm.org/doi/full/10.1056/NEJMp1211277?query=featured\\_home](http://www.nejm.org/doi/full/10.1056/NEJMp1211277?query=featured_home)

**Monday, October 15, 2012****Question:**

Acro-osteolysis, bony resorption of the terminal phalanges of the hands, has been associated with long standing occupational exposure to what chemical?

**Answer:**

Prolonged occupational exposure to high concentrations of vinyl chloride has been associated with the development of acro-osteolysis (among other problems). Acro-osteolysis has also been associated with scleroderma, psoriatic arthritis, direct injury, and certain hereditary syndromes. The development of acro-osteolysis associated with vinyl chloride may actually be due to chemically induced vascular insufficiency of the digits related to Raynaud's syndrome. (Ferreira IR and Domingue VS. Acro-osteolysis. 2012 Lancet 380:916)

**Friday, October 12, 2012****Question:**

What is pruno and what is the toxicological significance of pruno?

**Answer:**

Pruno is an illicit alcoholic beverage made with fruit, sugar, water and root vegetables such as potatoes. Pruno has recently been identified as the source for foodborne botulism in a group of incarcerated individuals. (MMWR October 5, 2012. Botulism from drinking prison made illicit alcohol. 61(39):782-784)

**Thursday, October 11, 2012**

**Question:**

What factors are most important in facilitating the fact that *Cryptosporidium* is the leading cause of reported treated recreational water associated outbreaks of gastroenteritis?

**Answer:**

Transmission via recreational water is facilitated by the substantial number of *Cryptosporidium* oocysts that can be shed by a single person, the extended periods of time that oocysts can be shed and the low infectious dose. However, perhaps the most important factor may be the tolerance *Cryptosporidium* oocysts display to chlorine used as a disinfectant. (MMWR September 7, 2012. *Cryptosporidiosis surveillance—United States, 2009–2010*. 61(5):11–12)

**Wednesday, October 10, 2012**

**Question:**

Clozapine is a dibenzodiazepine drug used to treat schizophrenia in patients who have not shown an adequate therapeutic response to at least two antipsychotic drugs. However, clozapine is associated with potentially serious side effects. What are these worrisome side effects?

**Answer:**

Clozapine is known to be associated with a variety of potentially life threatening effects including agranulocytosis, aspiration pneumonia, ileus, cardiomyopathy, and myocarditis. (Nielsen J, et al. Hematological clozapine monitoring with a point of care device: A randomized cross-over trial. 2011 *Euro Neuropsychopharm* 22(6):401–405)

**Tuesday, October 9, 2012**

**Question:**

Some resources recommend the topical application of vinegar to treat jellyfish stings in North America and Hawaii. Why may this not represent optimal therapy?

**Answer:**

A recent systematic review of the treatment of jellyfish stings in North America and Hawaii suggests “vinegar may not be an ideal agent because it causes pain exacerbation or nematocyst discharge in most species except *Physalia*”. The authors report that the application of lidocaine and hot water are the better treatment alternative but point out that these modalities may not always be available in the field. (Ward N, et al. Evidence-based treatment of jellyfish stings in North America and Hawaii. 2012 *Ann Emerg Med* 60(4):399–414)

**Monday, October 8, 2012**

**Question:**

The fluorinated pyrimidine, 5- fluorouracil, is often used in the topical treatment of actinic keratosis and certain superficial basal cell carcinomas. What is the clinical pharmacology that gives this drug efficacy against these clinical problems?

**Answer:**

According to the package insert for Efudex (fluorouracil) topical, there is evidence that the metabolism of fluorouracil in the anabolic pathway blocks the methylation reaction of deoxyuridylic acid to thymidylic acid. In this manner, fluorouracil interferes with the synthesis of DNA and to a lesser extent, RNA. Since DNA and RNA are essential for cell division and growth, the effects of fluorouracil may be to create a thymine deficiency that provokes unbalanced growth and death of the cell. The effects of DNA and RNA deprivation are most marked on those cells which grow more rapidly and take up fluorouracil at a more rapid rate. (Efudex package insert; Valeant Pharmaceuticals of North America)

**Friday, October 5, 2012**

**Question:**

What is Chan Su?

**Answer:**

Chan Su is a traditional Chinese medicine derived from the secretion of the skin and auricular glands of Chinese toads (*Bufo melanostictus* Schneider or *Bufo bufo* gargarzinas Gantor). It has been identified as an important component of various herbals and medicines used in Asia and elsewhere. Administration of Chan Su, traditionally given in small doses, is often aimed at stimulation of myocardial contraction and for the treatment of heart disease. It is also sometimes given as an analgesic and for the reduction of inflammation.

The cardiac effects of Chan Su probably result from its constituent bufadienolides, including bufalin. The cited reference reports: "Bufalin blocks vasodilatation and increases vasoconstriction, vascular resistance, and blood pressure by inhibiting Na, K-ATPase". Chan Su has also been reported to interfere with some serum digoxin assays. (Reyes MA et al. Effect of Chinese Medicines Chan Su and Lu-Shen-Wan on Serum Digoxin Measurement by Digoxin III, a New Digoxin Immunoassay. 2008 *Ther Drug Monitoring* 30(1):95–99)

**Thursday, October 4, 2012**

**Question:**

What are the conditions necessary to induce a Staph related food poisoning outbreak?

**Answer:**

The cited reference notes five conditions necessary to induce a Staph related food poisoning outbreak: “(1) a source containing enterotoxin-producing staphylococci: raw materials, healthy or infected carrier, (2) transfer of staphylococci from source to food, e.g., unclean food preparation tools because of poor hygiene practices, (3) food composition with favorable physicochemical characteristics for *S. aureus* growth and toxinogenesis, (4) favorable temperature and sufficient time for bacterial growth and toxin production, and (5) ingestion of food containing sufficient amounts of toxin to provoke symptoms”. (Hennekinne J, et al. *Staphylococcus aureus* and its food poisoning toxins: characterization and outbreak investigation. 2012 *FEMS Microbiol Rev* 36:815–836)

**Wednesday, October 3, 2012**

**Question:**

What is carbon black?



**Answer:**

Carbon black is also known as channel-black, furnace-black, thermal-black or lamp-black. Carbon black is produced from incomplete combustion of certain petroleum products including coal tar and similar products. It finds industrial use as a pigment and is also used in some heat absorbing applications as well as in some radar absorbing materials. IARC has classified carbon black as “possibly carcinogenic”, for humans (Group 2B). (Valberg PA et al. Integrating studies on carcinogenic risk of carbon black: epidemiology, animal exposures and mechanism of action. 2006 J Occ Env Med 48(12): 1291-1307)

**Tuesday, October 2, 2012**

**Question:**

What is the Wolff-Chaikoff effect?

**Answer:**

The cited article notes that “The inhibition of organic binding of iodide in the thyroid gland by excess iodide, resulting in the cessation of thyroid hormone synthesis, is known as the Wolff-Chaikoff effect.” (Heymann WR. Potassium iodide and the Wolff-Chaikoff effect: relevance for the dermatologist. 2000 Journal of the American Academy of Dermatology. 42(3):490-492)

**Monday, October 1, 2012**

**Question:**

Which electrolyte should be checked both before and during treatment with lithium? Why?

**Answer:**

The cited reference reports that as a result of a consistently high prevalence of hyperparathyroidism, serum calcium levels should be checked before and during treatment with lithium. (McKnight R et al. Lithium toxicity profile: a systematic review and meta-analysis. 2012 Lancet 379:721-728)

**Friday, September 28, 2012**

**Question:**

Acrodynia, first described in 1830, is a syndrome associated with exposure to elemental or inorganic mercury, most commonly in pediatric patients. This syndrome usually involves painful, erythematous desquamation of fingers and toes with local edema and neurological symptoms such as irritability, parenthesis and photophobia. In addition, acrodynia may be associated with the development of hypertension. What is the mechanism for the development of hypertension in the face of acrodynia?

**Answer:**

According to the cited references, mercury causes elevated blood pressure due to inhibition of catecholamine-O-methyltransferase, the critical enzyme involved in catabolism of catecholamines. This occurs via direct inactivation of a coenzyme, S-adenosylmethionine. Inhibition of catecholamine-O-methyltransferase by mercury results in accumulation of dopamine, epinephrine, and norepinephrine leading to hypertension. (Torres AD, et al. Mercury intoxication and arterial hypertension: report of two patients and review of the literature. 2000 Pediatrics105:E34 as cited in Mercer JJ, et al. Acrodynia and hypertension in a young girl secondary to elemental mercury toxicity acquired in the home. 2012 Pediatric Derm 29(2):199-201)

**Thursday, September 27, 2012**

**Question:**

DEET (N,N-diethyl-m-toluamide) is a topical insect repellent with well known efficacy against mosquitoes, ticks, chiggers, fleas, gnats and some flies. What is the DEET containing material known as EDTIAR?

**Answer:**

EDTIAR is “US Army Extended Duration Topical Insect and Arthropod Repellent”, was developed for the US military, and is marketed under the brand name Ultrathon lotion. This formulation contains 34% DEET and has been reported to provide protection for up to 12 hours. (The Medical Letter September 17, 2012, 54(12399):75-76)

**Wednesday, September 26, 2012**

**Question:**

How does heparin induced thrombocytopenia (HIT) differ from all other drug-induced thrombocytopenias?

**Answer:**

HIT is unique with regard to drug-induced thrombocytopenias because it requires platelet activation, rather than coagulation system activation to create the predisposing condition for thrombosis. (Bilen O and Teruya J. Complications of anticoagulation. 2012 Disease-a-Month 58(8):440-447)

**Tuesday, September 25, 2012**

**Question:**

What is the “pine nut syndrome”?

**Answer:**

Pine nut syndrome is a constellation of symptoms that reportedly develop 1-3 days after eating pine nuts (Pinus armandii) and is characterized by a variety of taste disturbances including the perception of a metallic taste or bitter taste in the mouth. According to the cited reference, other symptoms may include vomiting, headache, nausea and headache. (Ballin NZ A trial investigating the symptoms related to pine nut syndrome. 2012 J Med Toxicol 8(3): 278-230)

**Monday, September 24, 2012**

**Question:**

The mainstay of treatment for ethylene glycol poisoning involves inhibition of alcohol dehydrogenase using fomepizole in conjunction with hemodialysis. What is the elimination half-life of ethylene glycol in humans treated with fomepizole but who have not received hemodialysis?

**Answer:**

The study cited below reported that the mean elimination half-life of ethylene glycol in humans treated with fomepizole but who have not received hemodialysis was 14.2 hours (SD 3.7 hours; 95% CI 13.1 to 15.3 hours) Levine M. et al. Ethylene glycol elimination kinetics and outcomes in patients managed without hemodialysis. 2012 Ann Emerg Med 59:527-531)

**Friday, September 21, 2012**

**Question:**

What is Pa Ping?

**Answer:**

Pa Ping is a syndrome of barium-induced hypokalemia. Pa Ping was first identified in 1930 by Canadian medical missionary Dr. A. Stewart Allen who noticed an unusual pattern of illness in residents of Leshan, China, in patients presenting with nausea, vomiting, and diarrhea, and a gradual ascending paralysis occasionally causing death. Meals of patients with Pa Ping were found to contain barium in concentrations as high as 25.7%. The source of barium was theorized to be from faulty production processes for salt for food stuffs that contained barium chloride. (Bowen LN et al Elementary, my dear Dr. Allen. The case of barium toxicity and Pa Ping. 2010 Neurology 74: 1546-1549)

**Thursday, September 20, 2012**

**Question:**

What is the sensitivity and specificity of Chvostek's and Trousseau's signs with regard to hypocalcemia?

**Answer:**

The cited reference states "Chvostek's sign is neither sensitive nor specific for hypocalcemia, since it is absent in about one third of patients with hypocalcemia and is present in approximately 10% of persons with normal calcium levels. Trousseau's sign, however, is more sensitive and specific; it is present in 94% of patients with hypocalcemia and in only 1% of persons with normal calcium levels." (Jesus JE and Landry A. Chvostek's and Trousseau's signs. 2012 NEJM 367e15, September 13, 2012)

**Wednesday, September 19, 2012**

**Question:**

A 19-year-old female calls the poison center stating she received a tattoo on her upper arm one month ago and now has what sounds like red papules in and around the site of the tattoo. The tattoo consists of a large red rose and most of the ink used was bright red in color. What is the likely source of these red papules?

**Answer:**

Based on recent reports and cautions issued by the FDA, these red papules likely represent nontuberculous mycobacterial infection from contaminated tattoo ink. The caller should be referred to a knowledgeable dermatologist or other physician for treatment. The cited reference points out that "Antibiotic choices are limited by the susceptibility profile of the organism and prolonged treatment may be necessary to clear the infection." They go on to note that many persons treated with macrolides have had "favorable response" to this therapy. A recently reported outbreak found contaminated ink in an unopened container and "thus, contamination could have occurred at various points in the ink-production process-for instance, from unsanitary manufacturing processes or the use of contaminated ingredients such as water, glycerin or pigments." (LeBlanc PM et al. Tattoo ink-related infections-awareness, diagnose, reporting and prevention. 2012 NEJM 367(11):985-987)

**Tuesday, September 18, 2012**

**Question:**

The bacillus that causes the disease known as melioidosis is classified as a category B bioterrorism agent by the CDC. What is the causative organism for melioidosis? How does this organism enter the human body? What characterizes the clinical syndrome associated with this disease?

**Answer:**

The causative agent for melioidosis is *Burkholderia pseudomallei*. Infection with this organism usually occurs via percutaneous exposure from penetrating injury or via open wounds, via inhalation of air contaminated with the organism (especially during or after severe weather) or via the ingestion of contaminated water or food. The cited reference points out that this disease is seasonal in that 3/4 or more of all cases (not associated with deliberate release) occur during rainy seasons. The clinical syndrome associated with melioidosis typically involves the development of pneumonia and multiple abscesses involving multiple internal organs as well as skin. The incubation period is variable from 1 to 21 days and the disease has a mortality rate as high as 40%. (Wiersinga WK et al. Melioidosis (2012 NEJM 367(11): 1035-1044)

**Monday, September 17, 2012**

**Question:**

The FDA has recently requested revisions of labeling for the drug citalopram (Celexa and others). What do these revisions include?

**Answer:**

The FDA requested revisions include a decrease in the maximum daily dose of citalopram from 60 mg to 40 mg in most patients and to as low as 20 mg in selected other patients including those older than 60 years, those with hepatic impairment and those who are known to be CYP2C19 "poor metabolizers". In addition, the cited reference notes "The new label advises against use of citalopram in patients with congenital long QT syndrome and in those who are taking any of the many other drugs that prolong the QT interval." The drug is also specifically not recommended in those with recent myocardial infarction or uncompensated heart failure. (<http://www.fda.gov/Drugs/DrugSafety/ucm297391.htm> as referenced in The Medical Letter, 54(1398):71-72, September 3, 2012)

**Friday, September 14, 2012**

**Question:**

Which drugs are known to predispose to heat illness?

**Answer:**

The cited reference notes that the following drugs predispose individuals to heat illness: All typical antipsychotics, all atypical antipsychotics, all tricyclic antidepressants, atropine, benztropine, cyclobenzaprine, diphenhydramine, hydrochlorothiazide, furosemide, metoclopramide, methylphenidate, oxybutynin, prochlorperazine, promethazine, scopolamine, spirinolactone, amphetamines, cocaine., (Levine M et al. Influence of drug use on morbidity and mortality in heatstroke. 2012 J Med Tox 8(3): 252-257)

**Thursday, September 13, 2012****Question:**

What is the recommended treatment for acute onset, drug induced torsades de pointes?

**Answer:**

The cited reference notes “A bolus of 2 g 50% magnesium followed by a second bolus 5 to 15 minutes later if needed is effective in terminating most torsades de pointes episodes”. As an alternative, a continuous infusion of magnesium may be administered at 3-10 mg/min. Due to the risk of hypermagnesemia (interference with neuromuscular function), patients should be monitored closely. (Passman R and Kadish A. Polymorphic ventricular tachycardia, long Q-T syndrome and torsades de pointes. 2001 Medical Clinics of NA 85(2).

**Wednesday, September 12, 2012****Question:**

During the 1990’s, important longitudinal developmental studies were carried out in the Seychelles Islands and the Faroe Islands. The toxicological effects of what chemical were central to these studies?

**Answer:**

These classic studies were aimed at evaluating the developmental effects of methyl mercury derived from ingested fish. (National Research Council (NRC). (2000) Toxicological effects of methylmercury. Committee on the Toxicological Effects of Methylmercury, Board on Environmental Studies and Toxicology, Commission on Life Sciences, National Research Council. Washington, DC: National Academy Press.)

**Tuesday, September 11, 2012****Question:**

With regard to the clinical diagnosis of foodborne botulism, what are the so-called “Dozen D’s” and how do these findings play into the level of clinical suspicion for food borne botulism?

**Answer:**

The clinical signs and symptoms of foodborne botulism have been summarized as the “Dozen D’s”: Dry mouth; Diplopia; Dilated pupils; Droopy eyelids; Droopy face; Diminished gag reflex; Dysphagia; Dysarthria; Dysphonia; Difficulty lifting head; Descending paralysis; and Dyspnea from diaphragmatic paralysis. The cited reference states “botulism should be considered when three or more of the “Dozen D’s” are present”. (Horowitz BZ. Botulinum toxin 2005 Crit Care Clin 21:825-839 as cited in Vasa M, et al. The eyes have it. 2012 NEJM 367(11): 938-943)

**Monday, September 10, 2012****Question:**

Intravenously administered immune globulin (IVIG) is widely used in the treatment of a variety of immune-mediated disorders and is often used in the treatment of the Guillain-Barré syndrome. What specific hematologic problem has been associated with high doses of IVIG?

**Answer:**

The administration of IVIG in high doses has been reported to cause hemolytic anemia. This is an uncommon complication but nonetheless a potentially serious one. (Pintova S et al. IVIG-A hemolytic culprit. (Letter to the Editor) 2012 NEJM 367(10): 974-976)

**Friday, September 7, 2012****Question:**

“Bath salts” are designer drugs in the phenethylamine class. They are structurally similar to methcathinone. These substances can cause a variety of serious adverse effects including muscle spasms, hypertension, renal failure, seizures, hallucinations, aggression, severe paranoia, panic attacks, and hyperthermia. What are the most common active chemical ingredients contained in these potentially dangerous “bath salts”?

**Answer:**

The most common active ingredients contained in “bath salts” are methylenedioxypyrovalerone (MDPV) (3,4 methylenedioxypyrovalerone) and/or mephedrone (4-methylmethcathinone). (Fass JA et al. Synthetic cathinones (bath salts): Legal status and patterns of abuse. 2012 Annals of Pharmacotherapy 46:436-441)

**Thursday, September 6, 2012****Question:**

How is ziprasidone (Geodon) metabolized and how does the mechanism of metabolism of this drug minimize the possibility of adverse drug-drug interactions?

**Answer:**

Ziprasidone is metabolized by two enzymes in humans: cytochrome P4503A4 and aldehyde oxidase. The cited reference notes “Concerns surrounding pharmacokinetic drug interactions between ziprasidone and other drugs are diminished because (1) CYP3A4 mediates only one third of ziprasidone metabolism and (2) aldehyde oxidase activity is not known to be altered by co-administration of other drugs. Furthermore, neither of these enzymes is known to be subject to genetic polymorphism that results in functional consequences in drug metabolism.” (Beedham C. et al. Ziprasidone metabolism, aldehyde oxidase, and clinical implications. 2003 J Clin Psychopharmacol 23: 229–232)

**Wednesday, September 5, 2012****Question:**

Methylthionium chloride is the chemical name for an important antidote. What is the common name for Methylthionium chloride?

**Answer:**

Methylthioninium chloride is “methylene blue”, the treatment of choice for methemoglobinemia. Methylene blue is also known as “basic blue”, “chromosmon”, “Swiss blue”, “urolene blue”, and “bleu de methylene”, among a long list of other synonyms. (Hunter L, et al. Methaemoglobinaemia associated with the use of cocaine and volatile nitrites as recreational drugs: a review. Br J Clin Pharm 72(1):18-26

**Tuesday, September 4, 2012****Question:**

How does HF (hydrofluoric acid) cause the destruction of tissue?

**Answer:**

The cited reference describes two general mechanisms for tissue destruction related to HF. The authors point out that “the hydrogen ions cause a corrosive burn similar to other acid burns. This damage occurs immediately and results in visible tissue destruction.” They go on to point out “The second mechanism of tissue injury is liquefaction necrosis of deeper tissues. This occurs as the highly lipophilic fluoride ions penetrate tissue and alter cellular metabolism.” The latter type of damage is of greater clinical importance as it may continue for up to several days if untreated. (Stuke LE et al. Hydrofluoric acid burns: A 15-year experience.2008 29:893– 896)

**Monday, September 3, 2012****Question:**

Ifosfamide is an alkylating drug used in the treatment of a variety of malignancies. It is a structural analog of cyclophosphamide and published reports indicate that as many as 60% of patients receiving this drug may develop encephalopathy characterized by confusion and disorientation. What is the mechanism for the development of ifosfamide induced encephalopathy?

**Answer:**

The mechanism by which ifosfamide causes encephalopathy has not been proven however, it is posited to be related to the dechloroethylation of ifosfamide into chloroacetaldehyde. Chloroacetaldehyde exerts an inhibitory effect on the central nervous system similar to that of acetaldehyde. Interestingly, orally administered ifosfamide reportedly causes a higher incidence of encephalopathy than does ifosfamide given via the intravenous therapy. (Patel P. 2006 Ann Pharmacother 40:299-303)

**Friday, August 31, 2012****Question:**

What role does trimellitic anhydride (TMA) play as a potential occupational hazard?

**Answer:**

TMA is used in the production of paints, plastics, adhesives and varnishes. Workers may be exposed to TMA as a dust or fume in certain occupational settings where airborne TMA is converted to trimellitic acid, a strong respiratory irritant. The cited reference points out that “This low-molecular-weight chemical [TMA] is unique in that it is also capable of eliciting specific IgG- and IgE-mediated immune responses leading to asthma and other immune disorders. The most common immunologic clinical conditions described for TMA-IgE sensitized workers have been rhinitis and asthma. Once sensitized, symptoms can occur within minutes after TMA re-exposure.” (Bernstein JA et al. Is Trimellitic Anhydride Skin Testing a Sufficient Screening Tool for Selectively Identifying TMA-Exposed Workers With TMA-Specific Serum IgE Antibodies? 2011 JOEM 53(10):1122-1127)

**Thursday, August 30, 2012****Question:**

What are the clinical indicators for yellow phosphorus ingestion?

**Answer:**

The diagnosis is often presumptively and primarily based on history. The cited reference notes there are no specific tests to facilitate the diagnosis of yellow phosphorus ingestion or poisoning. Phosphorus blood levels are specifically not helpful. The authors point out: “if the history is unclear, a garlicky odor and luminescence of vomitus or stool may be helpful. Faint fumes emanating from the stool are called smoking stool syndrome”. (Ates M et al. Living donor liver transplantation for acute liver failure in pediatric patients caused by the ingestion of fireworks containing yellow phosphorus. 2011 Liver Transplantation 17:1286-1291)

**Wednesday, August 29, 2012****Question:**

What is the primary toxin of the Portuguese man-of-war (Physalia physalis) and what is the mechanism of action of the primary toxin of this creature?

**Answer:**

The primary toxin of the Portuguese man-of-war (Physalia physalis) is a glycoprotein of 240 kDa known as Physaliatoxin. This toxin acts as a potent cytotoxic and hemolytic toxin. The specific mechanism of action for this toxin has yet to be elucidated. (Labadie M, et al. Portuguese man-of-war (Physalia physalis) envenomation on the Aquitaine Coast of France: an emerging health risk. 2012 Clin Tox 50(7):567-570)

**Tuesday, August 28, 2012****Question:**

Transdermal rotigotone (Neupro) is a non-ergot dopamine agonist initially approved for the treatment of Parkinson’s disease. It was withdrawn from the US market in 2008. Why was this product withdrawn from the market?

**Answer:**

Transdermal rotigotone (Neupro) was withdrawn from the US market in 2008 because crystallization of the drug within the transdermal patch itself could have led to under-dosing of the medication. The drug in transdermal form has recently been re-introduced to the US market and is approved for the treatment of Parkinson’s disease as well as “moderate to severe” restless legs syndrome. (The Medical Letter August 20,2012, 54(1397):68)

**Monday, August 27, 2012**

**Question:**

Why might foreign-born pregnant females be at increased risk for lead poisoning?

**Answer:**

The cited reference notes that foreign-born pregnant women might be at increased risk for lead poisoning due to the use of certain foreign products that may contain lead and the possibility of increased bone stores of lead from past exposures. The authors point out that the body's demand for calcium increases during pregnancy to support fetal bone development, which might release bone stores of lead. In 2011, of the 205 New York City women reported to New York City Department of Health and Mental Hygiene (DOHMH) with BLLs  $\geq 10$   $\mu\text{g}/\text{dL}$ , 118 (58%) were pregnant, and 98 (83%) of the pregnant women were foreign-born (DOHMH, unpublished data, 2011). More than 70% of pregnant women with elevated BLLs interviewed by DOHMH in 2011 reported using foreign traditional or familiar products from their ancestral countries, such as cosmetics, medications, remedies, food, and pottery. The authors suggest that health-care providers should question pregnant women about their use of such products. (Lead poisoning in pregnant women who used ayurvedic medications from India — New York City, 2011–2012. MMWR August 24, 2012 / 61(33):641–646)

**Friday, August 24, 2012**

**Question:**

What is the genus and species of the plant known as Deadly Nightshade?

**Answer:**

The Deadly Nightshade is *Atropa belladonna*. The cited reference notes: "Extracted from the plant is the alkaloid atropine (dl-hyoscyamine) which was to prove a cornerstone in the study of autonomic pharmacology." (Lee MR. Solanaceae IV: *Atropa belladonna* Deadly Nightshade. 2007 J R Coll Physicians Edinb 37:77-84)

**Thursday, August 23, 2012**

**Question:**

So-called artisanal (small scale, independently operated, mining operations not usually associated with a formal mining company) gold mining, in South America and elsewhere, has resulted in environmental contamination, and human exposure to, what potentially hazardous heavy metal?

**Answer:**

Artisanal gold mining has resulted in environmental contamination with elemental mercury which is used in the amalgamation and extraction process for gold in these small mining operations. (Cordy P et al. Mercury contamination from artisanal gold mining in Antioquia, Colombia: The world's highest per capita mercury pollution. 2011 Sci Total Env 410-411:154-160)

**Wednesday, August 22, 2012**

**Question:**

What is "opium dross"?

**Answer:**

Opium dross is the residue of opium remaining after opium is smoked. The opium dross reportedly contains high concentrations of morphine. The cited reference notes as follows: "Mixing additional opium with the dross and then evaporating the mixture will heighten the narcotic effects. In South-East Asia, this is the practice among hill-tribes in the northern part of the Laos and in Vietnam. Opium dross or residue, known in Persian as "shireh," is an opium preparation which is known and used in several other countries such as Afghanistan, Pakistan, China, and some Southeast Asia. Moreover, both opium and opium dross are abused by either smoking (smokers would use a specially designed opium pipe) or by ingestion. (Noohi S, et al. A Comparative Study of Characteristics and Risky Behaviors Among the Iranian Opium and Opium Dross Addicts. 2011 J Addict Med 5:74-78)

**Tuesday, August 21, 2012**

**Question:**

Which form of mercury is found in the vaccine preservative thimerosal? Which vaccines, used in the US, still contain thimerosal?

**Answer:**

Ethyl mercury has been used as a preservative in some vaccines. Thimerosal is still found in the influenza vaccines but has essentially been removed from all other vaccines routinely used in the US. (Cao Y., et al. Efficacy of succimer chelation of mercury at background exposures in toddlers. 2011 J Pediatr 158:480-485)

**Monday, August 20, 2012**

**Question:**

What is the so-called "DRESS syndrome" and which culprit drug (or drugs) is/are most commonly associated with this clinical problem? What is the recommended treatment for the DRESS Syndrome?

**Answer:**

The Drug Reaction with Eosinophilia and Systemic Symptom Syndrome (DRESS Syndrome) is a severe systemic adverse drug-induced reaction usually involving fever, hyper-eosinophilia, hepatic involvement, and lymphadenopathy. Most cases are associated with carbamazepine or allopurinol however DRESS has been associated with at least 50 different drugs. Cessation of the suspected culprit drug as well as treatment with systemic corticosteroids is the generally recommended treatment for DRESS Syndrome. (Cacoub P, et al. The DRESS Syndrome: A literature review. 2011 Amer J Med, 124(7):588-597)

**Friday, August 17, 2012**

**Question:**

The so-called Daubert standard is used to help determine the admissibility of scientific evidence in federal courts of law in the United States. What were the allegations in the landmark case that established the Daubert standard?

**Answer:**

The cited reference notes that in the landmark case (Daubert v Merrell Dow Pharmaceuticals, 1993), the Plaintiffs alleged that Bendectin, an anti-nausea drug prescribed for pregnant females, was teratogenic. Two specific Plaintiffs, Jason Daubert and Eric Schuller, alleged that they were born with limb reduction defects induced by Bendectin taken by their respective mothers. (Fung F. Demystifying the role of expert witness for clinical toxicologists. 2012 Clin Tox 50&7:539-545)

**Thursday, August 16, 2012**

**Question:**

What is the effect of marijuana use on motor vehicle crash risk?

**Answer:**

A recent meta-analysis reported marijuana use is associated with a significantly increased risk of motor vehicle crash. The cited study reported “drivers who test positive for marijuana or self-report using marijuana are more than twice as likely as other drivers to be involved in motor vehicle crashes. The increased risk of crash involvement associated with marijuana use is generally consistent across studies that were conducted in different geographic regions and driver populations, used different research design approaches, and were based on different methods for measuring marijuana use.” (Li M. Marijuana use and motor vehicle crashes. 2012 Epidemiologic Reviews 34:65-72)

**Wednesday, August 15, 2012**

**Question:**

Both Lewisite and sulfur mustard are considered to be vesicant chemical warfare agents. What are the clinical differences in the skin lesions produced by each of these vesicants?

**Answer:**

The cited reference notes that the skin lesions produced by Lewisite differ from those of sulfur mustard in their pathology and development. The authors note “Topical Lewisite exposure is accompanied by immediate pain, compared to the delayed symptoms caused by sulfur mustard, and while the blisters produced by Lewisite tend to be much more severe than those produced by HD, they heal faster.” (Nelson P et al. Therapeutic effects of hypothermia on Lewisite toxicity. 2006 Toxicology 222(1):8-16)

**Tuesday, August 14, 2012**

**Question:**

What is cassava, what potentially harmful chemical is contained in cassava, and what disorder may result from the ingestion of improperly processed cassava?

**Answer:**

Cassava is a plant root harvested from August through October and is the main staple in a variety of rural African locales. So-called “bitter cassava”, is high in cyanogenic glucoside. Flour is produced from cassava roots which are then cooked and eaten as a porridge. Studies have shown “average total cyanogenic potential of 40–46 mg HCN equivalents/kg flour (fresh weight) in some samples of cassava”. The ingestion of cassava, in some cases, has been associated with a disorder known as konzo. The cited reference notes “Konzo is characterized by the sudden onset of irreversible spastic paraparesis, associated with prolonged high dietary cyanogenic glucoside consumption and a diet deficient in sulphur amino acids”. (Cliff J, et al. Konzo and continuing cyanide intoxication from cassava in Mozambique. 2011 Food Chem Tox 49:631-635)

**Monday, August 13, 2012**

**Question:**

What is “tiro”?

**Answer:**

Tiro is a Nigerian eye cosmetic and folk remedy that may have been responsible for recent lead exposure to a child. In a recent (but solitary) case report, a child with blood lead levels of approximately 13 micrograms per deciliter was posited to have been due to the application of tiro as a fine powder to the dermal surfaces of the child’s eyelids. Tiro is just one of many substances that have been applied to eyelids in various cultures and have been subsequently associated with lead exposure. (MMWR August 3, 2012, 61(30):574-576)

**Friday, August 10, 2012**

**Question:**

Neonatal abstinence syndrome (NAS) may result from maternal methadone maintenance therapy during pregnancy. What is the relationship between the severity of this syndrome and the maternal dose of methadone?

**Answer:**

A recent systematic review reported, surprisingly, that the severity of NAS did not appear to differ statistically in mothers taking high dose methadone maintenance versus those taking low dose therapy. (Cleary BJ et al. Methadone dose and neonatal abstinence syndrome-systematic review and meta-analysis. 2010 Addiction 105:2071-2084)

**Thursday, August 9, 2012**

**Question:**

What are the currently recognized absolute contraindications for the use of epinephrine in the treatment of anaphylaxis?

**Answer:**

While some physicians may be hesitant to administer epinephrine to elderly patients or those with underlying coronary artery disease or other cardiovascular problems, there are no currently promulgated strict absolute contraindications to the use of epinephrine for the treatment of anaphylaxis. Nonetheless, current literature warns that care regarding dosing should be exercised when administering epinephrine via the intravenous route to elderly individuals or those with underlying cardiovascular disease. (Jacobsen RC and Millin MG. The use of epinephrine for out-of-hospital treatment of anaphylaxis: Resource document for the National Association of EMS Physicians position statement. 2011 Prehosp Emerg Care 15:570-576)

**Wednesday, August 8, 2012**

**Question:**

The anxiolytic herbal, kava (Piper methysticum), is known to cause hepatotoxicity in some cases. What constituents of this plant material are thought to be responsible for the hepatotoxicity that has been reported to arise from the use of this herbal?

**Answer:**

The cited reference points out: “At present, of special interest as possible culprits for kava hepatotoxicity are pipermethystine and flavokavain B as constituents of the kava plant and mould hepatotoxins as suspected contaminants of the kava raw material”. (Teschke R et al. Herbal hepatotoxicity by kava: Update on pipermethystine, flavokavain B, and mould hepatotoxins as primarily assumed culprits. 2011 Digestive and Liver disease 43:676-681)

**Tuesday, August 7, 2012**

**Question:**

Sensori-neural hearing loss (SSHL) secondary to drug abuse has (been reported among intravenous drug abusers following the injection of) heroin. What are the posited causes for this phenomenon?

**Answer:**

Theories regarding possible causes for heroin-associated SSLH include effects of contaminants (and adulterants that may be present as well as the possibility of inhibitory effects of the drug on adenylate cyclase activity on opioid receptors within the cochlea itself. Others have posited that local hypoperfusion induced by opioid initiated vasospasm may be responsible. Some have suggested that heroin adulteration, specifically with quinine, is responsible however given the relatively small amounts of quinine involved, most believe that quinine is not the culprit. (Christenson BJ and Marjala ARP. Two cases of sudden sensorineural hearing loss after methadone overdose. 2010 Ann Pharmacother 44:207-2010)

**Monday, August 6, 2012**

**Question:**

K2, also known as "Spice" (street names include: Bilss, Black Mamba, Bombay Blue, Fake Weed, Genie, Spice, Zohai) is a mixture of herbs and spices that is typically sprayed with a synthetic compound chemically similar to THC, the psychoactive ingredients in marijuana. The chemical compounds typically include HU-210, HU-211, JWH-018, and JWH-073. K2 is commonly purchased in head shops, tobacco shops, various retail outlets, and over the Internet. It is often marketed as incense or "fake weed." What is the current legal status of K2 in the US?

**Answer:**

On March 1, 2011, DEA published a final order in the Federal Register temporarily placing five synthetic cannabinoids into Schedule I of the CSA. The order became effective on March 1, 2011. The substances placed into Schedule I are 1-pentyl-3-(1-naphthoyl) indole (JWH-018), 1-butyl-3-(1-naphthoyl) indole (JWH-073), 1-[2-(4-morpholinyl)ethyl]-3-(1-naphthoyl)indole (JWH-200), 5-(1,1-dimethylheptyl)-2-[(1R,3S)-3-hydroxycyclohexyl]-phenol (CP-47,497), and 5-(1,1-dimethyloctyl)-2-[(1R,3S)-3-hydroxycyclohexyl]-phenol (cannabicyclohexanol; CP-47,497 C8 homologue). This action is based on a finding by the DEA Administrator that the placement of these synthetic cannabinoids into Schedule I of the CSA is necessary to avoid an imminent hazard to the public safety. ([www.justice.gov/dea/pubs/abuse/drug\\_data\\_sheets/K2\\_Spice.pdf](http://www.justice.gov/dea/pubs/abuse/drug_data_sheets/K2_Spice.pdf))

**Friday, August 3, 2012**

**Question:**

Based on its structure, the popular muscle relaxant cyclobenzaprine (Flexeril) sometimes creates a false positive drug test with regard to which class of drugs?

**Answer:**

The tricyclic structure of the drug cyclobenzaprine, makes this drug structurally very similar to the tricyclic antidepressants. The cited author point out: "In addition to common structural aspects, cyclobenzaprine also shares a similar, although less severe, anticholinergic and cardiac overdose adverse effect profile with tricyclic antidepressants". (Van Hoey NM. Effect of cyclobenzaprine on tricyclic antidepressant assays. 2005 Ann Pharmacother 39:1314-1317)

**Thursday, August 2, 2012**

**Question:**

The World Anti-Doping Agency (WADA) prohibits the use of so-called "masking agents" that may interfere with athletic drug testing as is being performed at the current Summer Olympics in London. What are these prohibited masking agents?

**Answer:**

The WADA prohibited "masking agents" include: "Diuretics, probenecid, plasma expanders (e.g. glycerol; intravenous administration of albumin, dextran, hydroxyethyl starch and mannitol) and other substances with similar biological effect(s)". ([http://www.wada-ama.org/Documents/World\\_Anti-Doping\\_Program/WADP-Prohibited-list/WADA\\_Prohibited\\_List\\_2010\\_EN.pdf](http://www.wada-ama.org/Documents/World_Anti-Doping_Program/WADP-Prohibited-list/WADA_Prohibited_List_2010_EN.pdf))

**Wednesday, August 1, 2012**

**Question:**

What is "parachuting"?

**Answer:**

The cited reference reports that "parachuting" is "A technique known as "parachuting" involves wrapping ecstasy (3,4-methylenedioxymethamphetamine, MDMA) or methamphetamine in a wrapper and letting the ingested wrapper unravel like a parachute in the gastrointestinal tract slowly, releasing the enveloped drug." (Hendrickson RG et al. "Parachuting" Meth: A Novel Delivery Method for Methamphetamine and Delayed-Onset Toxicity From "Body Stuffing". 2006 Clin Tox 44:379-382)

**Tuesday, July 31, 2012**

**Question:**

Carnitine supplementation is often used to reverse metabolic abnormalities associated with valproic acid overdose as well as to speed up the resolution of hyperammonemia in that setting. What effect does carnitine have on the CNS depression that may accompany valproic acid overdose?

**Answer:**

The cited reference points out that clinical observations do not support the notion that carnitine hastens the recovery of consciousness in individuals with CNS depression secondary to valproic acid overdose. (Lheureux P and Hantson P. Carnitine in the treatment of valproic acid-induced toxicity. 2009 Clin Tox 47:101-111)

**Monday, July 30, 2012**

**Question:**

During World War II the British military developed a munition termed the "W-bomb" containing so-called Compound W. What was compound W?

**Answer:**

Compound W was ricin. This so-called W-bomb was never used. (Olsnes S. The history of ricin, abrin and related toxins. 2004 Toxicol 44:361-370)

**Friday, July 27, 2012**

**Question:**

How might cocaine use pre-dispose to acute aortic injury in some patients?

**Answer:**

The cited reference notes: "The aorta's intima is susceptible to sheer force injury from profound hypertension and tachycardia that may accompany cocaine abuse". In addition, cocaine may decrease aortic elasticity and increase apoptosis of aortic vascular smooth muscle cells. Further, the authors point out that "the accelerated atherosclerosis that occurs in long-term cocaine abusers, as well as those with concomitant smoking, may predispose cocaine-abusing patients to acute aortic syndromes." (Finkel J and Marhefka GD. Rethinking cocaine-associated chest pain and acute coronary syndromes. 2011 Mayo Clin Proc 86(12):1198-1207)

**Thursday, July 26, 2012**

**Question:**

Environmental exposure to thallium is possible via air, water and food sources. Which of these three routes is responsible for the greatest thallium exposures?

**Answer:**

The greatest environmental thallium exposure occurs by eating fruits and green vegetables that are grown at home and contaminated by thallium while growing. Thallium containing particles may be released into the atmosphere from coal-burning power plants, cement factories, and smelting operations. This thallium, in small quantities, falls onto fruit and vegetable gardens and is readily taken up into plants through the roots and thus may enter the food supply. (ATSDR (Agency for Toxic Substances and Disease Registry). Toxicological profile for thallium. U.S. Public Health Service; 1992 as cited in Peter ALJ and Viraraghavan T. Thallium: a review of public health and environmental concerns. 2005 Env International 31:493-501)

**Wednesday, July 25, 2012**

**Question:**

Volume depleted pediatric patients who receive NSAIDs are at risk for what potentially serious complication?

**Answer:**

Volume depleted pediatric patients who receive NSAIDs are at risk for the development of acute renal failure. (Matthews C, et al. Using NSAIDs in volume depleted children can precipitate acute renal failure. 2007 Arch Dis Child 92:524-526)

**Tuesday, July 24, 2012**

**Question:**

What is the most likely toxicologic mechanism of action of ingested antimony?

**Answer:**

The cited reference notes that the mechanism of action of ingested antimony is similar to that of arsenic. Specifically, they state "antimony is thought to inhibit the pyruvate dehydrogenase complex, thus preventing acetyl coenzyme A from entering the Krebs cycle with a subsequent lack of ATP production". In addition, it has been suggested that antimony also may inhibit succinic oxidase and pyruvate oxidase and phosphofructokinase. (Konstantopoulos WM, Burns Ewald M and Pratt DS. Case 22-2012- A 34 year old man with intractable vomiting after ingestion of an unknown substance. 2012 NEJM 367:259-268)

**Monday, July 23, 2012**

**Question:**

Which snake is the largest venomous snake in North America?

**Answer:**

The eastern diamondback rattlesnake (Crotalus adamanteus) is the largest rattlesnake in the world and the largest venomous snake in North America. (www.cinncinnatizoo.com)

**Friday, July 20, 2012**

**Question:**

Cranial nerve palsies are, on occasion, associated with ethylene glycol poisoning. How quickly can one expect resolution of bulbar, facial or trigeminal palsies associated with ethylene glycol poisoning?

**Answer:**

The cited reference notes that bulbar, facial or trigeminal cranial nerve palsies may take as long as several months to resolve. (Glossop AJ and Bryden DC. Case report: An unusual presentation of ethylene glycol poisoning. 2009 J Intensive Care Soc 10(2):118-121)

**Thursday, July 19, 2012**

**Question:**

Diplopia has been reported on occasion following use of, and/or withdrawal from use of, which drug of abuse?

**Answer:**

The use of, and/or withdrawal from use, of heroin has been reported to be associated with diplopia in some individuals. According to the cited reference, "the incidence of diplopia and/or blurred vision during withdrawal among soldiers returning from Vietnam was reported as between 10% and 33.3%, depending on the mode of heroin use" (Firth AY. Heroin and diplopia. 2005 Addiction 100:46-50)

**Wednesday, July 18, 2012**

**Question:**

Colchicine has been used to treat gout for hundreds of years. However the drug is known to have a narrow therapeutic range. The recognized maximum cumulative IV dose is 4 mg for a single course of therapy, with a 7-day colchicine-free interval after each full IV course. However, deaths have been reported with cumulative doses as low as 5.5 mg. Which subset of patients have been identified as being a higher risk for toxicity and death due to the use of IV colchicine?



**Answer:**

Older adults, patients with preexisting renal and hepatic failure, and patients with concomitant use of nonsteroidal anti-inflammatory drugs or oral colchicine might have a higher risk for toxicity and death from IV colchicine. (Bonnell RA et al. Deaths associated with inappropriate intravenous colchicine administration. 2002 J Emerg Med 22:385-387 as cited in Centers for Disease Control and Prevention. Deaths from Intravenous Colchicine Resulting from a Compounding Pharmacy Error — Oregon and Washington, 2007 MMWR Oct 12,2007 56(40):1050-1052)

**Tuesday, July 17, 2012****Question:**

What is the only starfish known to contain a toxin?

**Answer:**

The crown-of-thorns starfish (*Acanthaster planci*) contains plancitoxins I and II, which have been reported to be associated with life-threatening hepatic toxicity. (Sato H, et al. Case of skin injuries due to stings by crown-of-thorns starfish (*Acanthaster planci*) 2008 J of dermatology 35:162-167)

**Monday, July 16, 2012****Question:**

Pennyroyal oil is derived from the leaves of the plant *Mentha pulegium*. Ingestion of pennyroyal oil has been used to induce abortion or to regulate menses by herbalists and others. Ingestion of this oil has been reported to cause massive and life-threatening necrosis of what human organ? What is the harmful chemical component responsible for this effect?

**Answer:**

Pennyroyal oil contains approximately 85% pulegone. Pulegone is a cyclohexanone in structure and is responsible for the liver damage associated with pennyroyal ingestion either by a direct toxic effect or in combination with a toxic metabolic intermediate epoxide and/or furan chemical. (Sullivan JB et al. Pennyroyal oil poisoning and hepatotoxicity. 1979 JAMA 242(26): 2873-2874)

**Friday, July 13, 2012****Question:**

What is CSF lavage and under what circumstances might this procedure be useful in treating a poisoned patient?

**Answer:**

CSF lavage is a procedure whereby 20-30 mL of CSF is removed and replaced with 30–40 mL of preservative-free normal saline or lactated Ringer's solution via an epidural catheter. This procedure may be considered (in conjunction with the use of appropriate reversal agents such as naloxone) in the face of serious opioid toxicity following therapeutic overdose due to intrathecal pump malfunction. CSF lavage has also been used to treat accidental therapeutic vincristine overdose. (Boyer EW. Management of opioid analgesic overdose. 2012 NEJM 367(2):146-155 and Tsui BC et al. Reversal of an unintentional spinal anesthetic by cerebrospinal lavage. 2004 Anesth Analg 98:434-436 and)

**Thursday, July 12, 2012****Question:**

Clenbuterol is a beta 2 adrenergic agonist agent that has been noted as an adulterant in heroin and other street drugs. Why has this drug also been abused by bodybuilders?

**Answer:**

Bodybuilders have reportedly used clenbuterol because, as the cited reference points out, this agent has “specific anabolic activity and increased lipolysis that is not seen with other beta agonists” with the ultimate goal of increasing lean muscle mass. (Yen M and Burns Ewald M. Toxicity of weight loss agents. 2012 J Med Toxicol 8(2):145-152)

**Wednesday, July 11, 2012****Question:**

What is food dependent-exercise -induced anaphylaxis?

**Answer:**

Food dependent-exercise -induced anaphylaxis is a rare form of anaphylaxis where patients are able to tolerate both a causative food and exercise separately but when combined an anaphylactic reaction ensues. The most common culprit foods include nuts, seafood and grains however wheat and wheat containing products are the most common instigator. (Keet C. Recognition and management of food induced anaphylaxis. 2011 Pediatr Clinics of North America 58(2))

**Tuesday, July 10, 2012****Question:**

The use and popularity of electronic cigarettes (e-cigarettes) is increasing. What chemicals have been reported to emanate from the mists generated from these “artificial” cigarettes?

**Answer:**

Several analyses have shown that nicotine, propylene glycol, diethylene glycol, a variety of N-nitrosamines, as well as several tobacco specific impurities suspected of being harmful to humans, including anabasine, myosmine, and Beta-nicotyrine may be present in the mist generated by electronic cigarettes. (Flouris AD and Oikonomou DN Electronic cigarettes: miracle or menace? 2010 Br Med J 340:23)

**Monday, July 9, 2012****Question:**

The leading cause of late death following cardiac transplantation is cancer. What effect might statin use have on malignancy in this group of patients?

**Answer:**

According to the cited reference, it is posited (but not yet proven) that “statin use is associated with improved cancer-free and overall survival after cardiac transplantation.” (Frohlich GM et al. Statins and the risk of cancer after heart transplantation. 2012 Circulation published online accessed at <http://circ.ahajournals.org/>)

**Friday, July 6, 2012**

**Question:**

Some commercially available products include so-called bittering chemicals that act as aversive agents to discourage the intentional ingestion of potentially harmful products. What is the most commonly used bittering agent used for this purpose?

**Answer:**

Denatonium benzoate is the most commonly used bittering agent. The cited reference notes that this agent can be perceived at concentrations as low as 50 parts per billion. (White NC et al. The impact of bittering agents on suicidal ingestions of antifreeze. 2008 Clin Tox 46(6):507-514)

**Thursday, July 5, 2012**

**Question:**

Sodium azide is an odorless, tasteless, water-soluble crystalline powder that has been used in the manufacture of automobile airbags, explosives, and as a laboratory preservative. During the 1950's sodium azide was used to treat hypertension because of its profound vasodilatory effects, posited to result in the production of nitric oxide. What are the potential adverse clinical effects associated with the systemic absorption of sodium azide and what treatments are recommended for sodium azide toxicity?

**Answer:**

Systemic absorption of sodium azide can result in hypotension, loss of consciousness, headache, dyspnea, nausea, vomiting, metabolic acidosis, dysrhythmias and death. The mechanism of poisoning with sodium azide is thought to be similar to cyanide, which suggests the use of traditional cyanide antidotes might be beneficial. However no controlled clinical trials have verified this and thus excellent supportive care remains the cornerstone of treatment. (Sodium azide poisoning at a restaurant-Dallas County, Texas,2010. MMWR June 29,2012; 61(25):457-460)

**Wednesday, July 4, 2012**

**Question:**

A patient presents with severe acute hypokalemia (K less than 2.0) following the ingestion of a fireworks product at a Fourth of July celebration. What component of the ingested fireworks is the most likely cause for this electrolyte abnormality?

**Answer:**

The most likely component to have caused this profound hypokalemia is barium chlorate, a common component of a variety of fireworks. Barium chlorate is responsible for imparting a green color when the firework is ignited. (Rhyee SH and Heard K. Acute barium toxicity from ingestion of "snake" fireworks. 2009 J Med Tox 5(4):209-213)

**Tuesday, July 3, 2012**

**Question:**

A patient presents with severe acute hypokalemia (K less than 2.0) following the ingestion of a fireworks product at a Fourth of July celebration. What component of the ingested fireworks is the most likely cause for this electrolyte abnormality?

**Answer:**

The most likely component to have caused this profound hypokalemia is barium chlorate, a common component of a variety of fireworks. Barium chlorate is responsible for imparting a green color when the firework is ignited. (Rhyee SH and Heard K. Acute barium toxicity from ingestion of "snake" fireworks. 2009 J Med Tox 5(4):209-213)

**Monday, July 2, 2012**

**Question:**

Following death, does fentanyl continue to be released into the circulation from pre-mortem, cutaneous placed, transdermal fentanyl patches?

**Answer:**

The cited reference states "There are no data to support continued postmortem release of fentanyl from TD patches from one part of the body (e.g.,the shoulder) causing an increase in blood fentanyl concentration in a distant anatomic site (e.g., the femoral vessels)." The author further points out "in the absence of circulation, there is no thermodynamic force to drive such a continued release. The movement of drug from the patch into the skin and subsequent systemic delivery requires continual uptake of fentanyl by the circulating blood. In the absence of circulatory uptake, the depot of drug in the skin will simply remain in equilibrium with the drug in the patch resulting in a net-zero transfer." (Palmer RB. Fentanyl in postmortem forensic toxicology. 2010 Clin Tox 48(8):771-784)

**Friday, June 29, 2012**

**Question:**

Exanthematous drug eruptions, also known as maculopapular drug rashes, are pruritic dermal reactions that usually occur between 4 and 21 days after an individual begins taking a given drug. What percent of first time users of any given drug will develop exanthematous drug rashes?

**Answer:**

Exanthematous drug eruptions can be expected to occur in 1-5% of first time users of any given drug. (Stern RS. Exanthematous drug eruptions. 2012 NEJM 366(26):2492-2501)

**Thursday, June 28, 2012**

**Question:**

Anascorp is an IV antivenom approved by the FDA for the treatment of scorpion envenomation. From where is this agent derived?

**Answer:**

Anascorp is derived from purified F(ab)2 fragments of equine IgG. The cited reference notes that "Venom from 4 Centroides species is used to immunize horses. After extraction, digestion, fractionation and purification, the product contains, according to the manufacturer, less than 5% intact immunoglobulin." According to recent studies, Anascorp is highly effective in the treatment of neurotoxicity related to scorpion envenomation with symptoms resolving in most patients in less than 2 hours following administration. (The Medical Letter 54(1393): 51-52 and Boyer LV et al. Antivenom for critically ill children with neurotoxicity from scorpion stings. 2009 NEJM 360:2090)

**Wednesday, June 27, 2012**

**Question:**

In the US, there are currently two treatment options for botulism in addition to airway management and supportive care. What are these two options and from where are they derived?

**Answer:**

In addition to airway management and supportive care the two treatment options for botulism are Trivalent (A,B,E) Antitoxin and Botulism Immune Globulin Intravenous-Human (BabyBig). The Trivalent preparation is derived from equine sources and the BabyBig is derived from human sources. (Brent J. The many faces of botulinum toxin. [Abstract] 2012 Clin Tox 50(5):451-451)

**Tuesday, June 26, 2012**

**Question:**

Codeine is a commonly used analgesic. What is the mechanism of action for this drug?

**Answer:**

Codeine acts as a prodrug that is enzymatically converted to morphine, the source for analgesia related to codeine. Codeine is bio- transformed to morphine via the action of cytochrome CYP2D6. The cited reference notes that roughly 7% of Caucasians are noted to be poor metabolizers of codeine due to a lack of functional activity for the CYP2D6. These individuals do not generally receive adequate analgesia from codeine. (Juurlink DN et al. Postpartum maternal codeine therapy and the risk of adverse neonatal outcomes: A retrospective cohort study. 2012 Clin Tox 50(5):390-395)

**Monday, June 25, 2012**

**Question:**

Individuals suffering from toxicity related to the use of levamisole-adulterated cocaine often present with cutaneous manifestations. What are the typical cutaneous manifestations in this setting?

**Answer:**

The cutaneous manifestations associated with levamisole-adulterated cocaine use include large and painful hemorrhagic bullae with or without skin necrosis. The cited reference points out that these manifestations are commonly seen on the face and are often present bilaterally on the aural helices and the cheeks. (Lee KC et al. Complications associated with use of levamisole-contaminated cocaine: An emerging public health challenge. 2012 Mayo Clin Proc 87(6): 581-585)

**Friday, June 22, 2012**

**Question:**

Mees' lines are characteristically associated with exposure to what toxicant?

**Answer:**

Mees' lines are usually described in association with arsenic toxicity; however, they have also been described in association with exposure to thallium, in chronic kidney disease, in some cases of congestive heart failure, and in association with treatment with certain chemotherapy drugs.

Mees' lines do not represent deposition of any chemical within the nail. Rather, these horizontal white lines form secondary to dysfunctional growth at the nail matrix after a systemic insult and grow distally with time if the insult is removed. (Podjasek JO and Cook-Norris RH. Mees' lines. 2010 Clin Tox 48:958)

**Thursday, June 21, 2012**

**Question:**

In 1982, Accutane, 13-cis-retinoic acid (isotretinoin), appeared on the U.S. market for the treatment of severe cystic acne. Several years later the teratogenic potential of this medication was realized. What are the teratogenic risks associated with this drug, what is the characteristic pattern of fetal malformations associated with this drug and what are the most prominent craniofacial malformations reported to be associated with this drug?

**Answer:**

The cited reference notes that human exposure risks associated with therapeutic dosing during embryogenesis are: 40% for spontaneous abortion, 4–5% for perinatal mortality, 16% for premature birth, and 25% for major malformations. The characteristic pattern of malformations has been reported to include craniofacial, cardiac, thymic, and CNS structures. The cited reference further points out "The most striking craniofacial features [associated with isotretinoin] were ear malformations and cranial motor nerve (oculomotor and facial) abnormalities, which were typically asymmetric". (Adams J. The Neurobehavioral Teratology of Retinoids: A 50-Year History. 2010 Birth Defects Research (Part A) 88:895-905)

**Wednesday, June 20, 2012**

**Question:**

Constipation has been reported to occur in 40% or more of patients on hemodialysis. How does this fact influence the pre-disposition of dialysis patients to hyperkalemia?

**Answer:**

The cited reference notes that the amount of potassium excreted through the GI tract is proportional to the volume of stool. Another study (Sugarman and Brown, 1988) reported that the "24 hours fecal potassium excretion in anephric dialysis patients to be less than 5 mmol on a 40 mmol/day potassium diet. (Ahmed J and Weisberg LS. Hyperkalemia in dialysis patients. 2001 Seminars in Dialysis 14(5):348-356 and Sugarman A and Brown RS. The role of aldosterone in potassium tolerance: studies in anephric humans. 1988 Kidney Int 34:397-403)

**Tuesday, June 19, 2012**

**Question:**

Toxicity related to which heavy metal should be included in the differential diagnosis of Guillain-Barre syndrome?

**Answer:**

Arsenic should be included in the differential diagnosis of Guillain-Barre syndrome. As the cited reference points out, arsenic neurotoxicity "is usually a symmetrical sensorimotor neuropathy, often resembling the Guillain-Barré syndrome". Arsenic-related neuropathy is usually an ascending phenomenon, similar to what is often seen in the Guillain-Barré syndrome. (Vahidnia A et al. Arsenic neurotoxicity-A review. 2007 Human & Experimental Toxicology 26: 823-832)

**Monday, June 18, 2012**

**Question:**

Extensive intra-cranial calcifications on CT scan have been reported in association with cronic toxicity of which heavy metal?

**Answer:**

Extensive intra-cranial calcifications on CT scan have been reported in association with chronic lead intoxication. (Atre AL, et al. Pre and post treatment MR imaging findings in lead encephalopathy. 2006 Am J Neuroradiology 27:902-903)

**Friday, June 15, 2012**

**Question:**

What are organotins, where have they been coommonly used, and what environmental issues have the use of products containing these chemicals raised?

**Answer:**

Organotins are a class of chemicals with strong biocidal activity. The tri-substituted organotins, specifically tributyltin and triphenyltin, have been used extensively in antifouling marine paints as well as in the agricultural industry. The cited reference notes "Due to decades of leaching from antifouling paints applied on boat hulls and other underwater structures, tributyltin and triphenyltin have caused serious environmental problems in many harbors and dockyards worldwide." Since organotins tend to bio accumulate in marine ecosystems eating fish contaminated by organotins may pose a health risk for humans. (Airaksinen R. Organotin intake through fish consumption in Finland. 2010 Env Research 110:544-547)

**Thursday, June 14, 2012**

**Question:**

What are "poppers" and under what circumstances are are poppers used?

**Answer:**

"Poppers" are volatile nitrites; aliphatic esters of nitrous acid. They have a distinctly sweet odor and are typically used via inhalation. The cited reference indicates "Their vasodilatory effects were first described in 1859 and subsequently, they were used in the treatment of angina from 1867. During the 1960s nitrates replaced their use in the treatment of angina and abuse of nitrites became widespread". Poppers were so-named as a result of a popping noise made when glass vials containing the substance were crushed just before inhalation. The cited reference notes that poppers are "sold in men who have sex with men (gay) clubs, sex shops and in head shops. They are sold in small glass bottles containing 10–30 ml, under a variety of trade names including 'Rush', 'Liquid Gold' and 'TNT'." The authors go on to describe the use of poppers as "popular among men who have sex with men, due to their aphrodisiac and vasodilatory properties. They are inhaled either during foreplay to obtain a high and produce relaxation of the anal sphincter, or just preceding orgasm to prolong climax. Poppers have also been inhaled by dipping cigarettes into the liquid. Because of the high flammability of nitrites, inadvertent lighting of these cigarettes at a later time, risks severe burns." (Hunter L, et al. Methaemoglobinaemia associated with the use of cocaine and volatile nitrites as recreational drugs: a review. 2011 Br J Clin Pharm 72(1):18-26)

**Wednesday, June 13, 2012**

**Question:**

Linezolid is an antibiotic of the oxazolidinone class. This drug has known activity against gram-positive cocci, including MRSA (methicillin-resistant Staphylococcus aureus). Linezolid has been reported to cause a potentially life threatening metabolic abnormality in some cases. What is this abnormality and what is the mechanism theorized to be at play in this setting?

**Answer:**

The cited reference notes that Linezolid has been reported to induce lactic acidosis, "especially after prolonged administration, through inhibition of the mitochondrially synthesized components of oxidative phosphorylation". (Cope TE, et. at. Rapid-onset, linezolid-induced lactic acidosis in MELAS. 2011 Mitochondrion 11:992–993)

**Tuesday, June 12, 2012**

**Question:**

Chewing the leaves of the Catha edulis (Khat) plant results in the release of cathinone, (an amphetamine-like compound). The chewing of Khat, as a stimulant, is especially popular in some countries in northern Africa and the Middle East. Khat chewing is also practiced by some individuals who have immigrated to the US from these areas. Chronic chewing of Khat has been associated with an increased risk for what specific medical problems?

**Answer:**

Chewing Khat has been associated with an increased risk for myocardial infarction, dilated cardiomyopathy and duodenal ulcers. (Al-Motarreb A, et al. Khat chewing, cardiovascular disease and other internal medical problems; the current situation and directions for future research. 2010 J Ethnopharmacol 132:540–548 as cited in Prosser JM and Nelson LS. The toxicology of bath salts: A review of synthetic cathinones. 2012 J Med Toxicol 8:33-42)

**Monday, June 11, 2012**

**Question:**

What neuropsychiatric symptoms have been reported to be associated with ciguatera fish poisoning?

**Answer:**

The neuropsychiatric symptoms that have been reported (but not proven) in association with ciguatera fish poisonign include anxiety, depression, subjective memory loss, hallucinations, "giddiness", ataxia and coma. (Friedman MA et al. Ciguatera fish poisoning: tretamnet, prevention and management. 2008 Marine Drugs 6:456-479)

**Friday, June 8, 2012**

**Question:**

According to the Women's Health Initiative study women taking estrogen plus a progestin for more than 5 years were at increased risk for what medical problems?

**Answer:**

According to the Women's Health Initiative study women taking estrogen plus a progestin for more than 5 years were at increased risk for coronary heart disease, stroke, venous thromboembolism, and breast cancer. (JE Manson et al. Estrogen plus progestin and the risk of coronary heart disease 2003 NEJM 349:523 as cited in The Medical Letter. Drugs for menopausal symptoms. 2012; 54(1391):41-43)

**Thursday, June 7, 2012**

**Question:**

Tick paralysis is a tick-borne disorder caused by a toxin (not by an infectious disease). This disorder involves acute flaccid paralysis due to a neurotoxin injected from the salivary glands of female ticks attached and feeding on a human blood meal. How long must the female tick be attached and feeding before paralysis occurs?

**Answer:**

According to the cited reference, paralysis does not occur until female ticks have been feeding for at least 4 to 5 days. (Greenstein P. Tick paralysis. 2002 Med Clin No Amer 86(2):441-446 as cited in Decker CF et al. Tick-Borne Illnesses. 2012 Disease-a-Month 58(6):3121-388)

**Wednesday, June 6, 2012**

**Question:**

What drug is the only FDA approved treatment for HIT (heparin induced thrombocytopenia) currently marketed in the US?

**Answer:**

Argatroban is the only FDA approved treatment for HIT (heparin induced thrombocytopenia) currently marketed in the US. (The Medical Letter. Choice of drugs for heparin-induced thrombocytopenia 54(1391):43-44)

**Tuesday, June 5, 2012**

**Question:**

In patients receiving digoxin, which cardiac arrhythmias are generally considered to be digoxin-toxic rhythms unless proven otherwise?

**Answer:**

Those rhythms that are generally considered to be digoxin-toxic rhythms unless proven otherwise are 1) new-onset Mobitz type I AV block (Wenckebach periodicity), 2) accelerated junctional rhythm with or without high-degree AV block, 3) non-paroxysmal atrial tachycardia with AV block, and 4) bidirectional ventricular tachycardia. (Bauman JL et al. Mechanisms, manifestations and management of digoxin toxicity in the modern era. 2006 Am J Cardiovasc Drugs Mar.-Apr. 2006: 77+. Academic OneFile. Available at [http://go.galegroup.com.ezproxy2.library.drexel.edu/ps/i.do?id=GALE%7CA199464027&v=2.1&u=drexel\\_main&it=r&p=AONE&sw=w](http://go.galegroup.com.ezproxy2.library.drexel.edu/ps/i.do?id=GALE%7CA199464027&v=2.1&u=drexel_main&it=r&p=AONE&sw=w))

**Monday, June 4, 2012**

**Question:**

Heparin treatment may be associated with unexplained hyperkalemia in some patients. What is the proposed mechanism for heparin induced hyperkalemia?

**Answer:**

The cited reference points out that even when given in small doses (subcutaneously or IV), "heparin has been reported to decrease plasma aldosterone concentrations, leading to increases in measured serum potassium levels. The mechanism is thought to be attributable to direct inhibition of the adrenal gland's zona glomerulosa, with selective reduction in aldosterone production." It is important to note that hyperkalemia has also been reported associated with low-molecular-weight heparin, consequently switching to this form of heparin may not represent an optimal strategy. (Hickson LJ et al. Clinical pearls in nephrology. 2010 Mayo Clin Proc 11:1046-1050)

**Friday, June 1, 2012**

**Question:**

Shigella is a toxin-producing bacteria often spread via contaminated food or water. Infection with Shigella is well known to be associated with the development of seizures that can be seen in as many as 30% of cases. What is the mechanism for Shigella-related seizures?

**Answer:**

Seizures and/or altered mental status and are not believed to be caused specifically by Shiga toxin however the precise mechanism for Shigella-related seizures remains unproven. The cited reference points out that in this regard, hypotheses for the etiology of Shigella-related seizures include "high rate of temperature elevation, induction of cerebral edema, increased levels of corticotropin-releasing hormone, nitric oxide, and/or the cytokines tumor necrosis factor alpha and interleukin 1beta induced by Shigella infection.(Goldberg EM et al. Seizure and altered mental status in a 12-Year-Old Child with Shigella sonnei gastroenteritis. 2011 Ped Emerg Care 27(2):135-137)

**Thursday, May 31, 2012**

**Question:**

Many clinicians refrain from treating young children with tetracycline drugs due to concerns about the possibility of tooth staining. Is this concern supported by the literature?

**Answer:**

Studies in the 1960s and 70s reported that repeat administration of tetracycline to infants and young children was associated with staining of developing teeth. Later studies showed that the use of doxycycline was only negligibly associated with staining of developing teeth. The below cited reference reported no tooth staining in children (mean age 4.1 years) following an average of 2 courses of treatment with doxycycline in children under 8 years of age. (Volovitz B et al. Absence of tooth staining with doxycycline treatment in young children. 2007 Clin Pediatr 46(2):121-126)

**Wednesday, May 30, 2012**

**Question:**

What are "pumping parties"?

**Answer:**

"Pumping parties" involve a popular (and growing in popularity) underground and illicit cosmetic surgical intervention where individuals receive one or more injections of liquid silicone administered by non-qualified individuals. The most common anatomical sites for such injections are the face, breast, vagina, buttocks and hips. Significant local as well as systemic complications (including death) have been reported as a result of the use of silicone at such "pumping parties". (Bartsich S and Wu JK. Silicon emboli syndrome: A sequel of clandestine liquid silicone injections. A case report and review of the literature. 2010 J Plastic Recon Aesthetic Surg 63: e1-e3)

**Tuesday, May 29, 2012**

**Question:**

DEET (N,N-diethyl-meta-toluamide) containing insect repellent products come in a variety of concentrations up to 30 % DEET. Why are Products containing greater than 30% DEET not recommended for routine use?

**Answer:**

Products containing more than 30% DEET provide only negligible additional protection beyond that conveyed by products containing no more than 30% DEET. (CDC. Insect repellent use and safety, 2010. Available at: [http://www.cdc.gov/ncidod/dvbid/westnile/qa/insect\\_repellent.htm](http://www.cdc.gov/ncidod/dvbid/westnile/qa/insect_repellent.htm).)

**Monday, May 28, 2012**

**Question:**

Envenomation by stonefish (family Synanceiidae) are reported to be intensely painful and envenomation by these marine creatures can be fatal. What are the toxic components of stonefish venom? What is the recommended treatment for the pain associated with stonefish envenomation?

**Answer:**

Stonefish venom contains elements associated with cardiovascular, neuromuscular and cytolytic toxicities. Specifically stonefish venom contains trachynilysin ( a neurotoxin) and cardiopleutin ( a catecholamine-like cardiotoxic chemical). Prentice et al point out that "Stonefish venom is heat labile, and immersion of the affected area in hot water should provide pain relief. The water should be as hot as can be tolerated without scalding (42°C- 45°C), and immersion should be continued until pain resolves, often for several hours, and repeated with return of pain. Along with hot water immersion, oral or parenteral opioid analgesics may be required to control the severe pain." (Church JE and Hodgson WC. The pharmacological activity of fosh venoms. 2002 Toxicon 40:1083-1093 as cited in Prentice O et al. Stonefish envenomation 2008 Am J Emerg Med 26: 972.e1-972.e2)

**Friday, May 25, 2012**

**Question:**

What is the pathologic mechanism of caterpillar-associated skin rashes?

**Answer:**

The pathologic mechanism of caterpillar-associated rash is not understood entirely and depends on the caterpillar species. The mechanism is thought to involve exposure to chemicals on caterpillar or cocoon hairs (spicules) or mechanical irritation. Additionally, when caterpillars and cocoons are in high density, particularly susceptible persons can develop a rash when the hairs become airborne. In these situations, the rash might not occur on the area of the skin where caterpillar or cocoon contact occurred. (MMWR. Caterpillar-associated rashes in children. March 30,2012 61(12):209-211)

**Thursday, May 24, 2012**

**Question:**

Is it safe to use cephalosporin antibiotics for patients with a history of penicillin allergy?

**Answer:**

The cited references notes " .....a myth persists that approximately 10% of patients with a history of penicillin allergy will have an allergic reaction if given a cephalosporin.....the overall cross-reactivity rate is actually approximately 1% when using first generation cephalosporins or cephalosporins with similar R1 side chains. For penicillin-allergic patients, the use of 3rd or 4th generation cephalosporins or cephalosporins with dissimilar side chains than the offending penicillin carries a negligible risk of cross allergy." (Campagna JD et al. The use of cephalosporins in penicillin allergic patients: A literature review. 2012 J Emerg Med 42(5):612-620)

**Wednesday, May 23, 2012**

**Question:**

Azithromycin has been reported to be pro-arrhythmogenic in a number of studies. What arrhythmias have been associated with the use of azithromycin and what duration of azithromycin therapy has been associated with an increase risk of cardiovascular death?

**Answer:**

The arrhythmias that have been associated with the use of azithromycin include pronounced QT –interval prolongation, torsade de pointes, and polymorphic ventricular tachycardia. The cited reference reports "During 5 days of therapy, patients taking azithromycin as compared with those who took no antibiotics, had an increase risk of cardiovascular death." (Ray WA et al. Azithromycin and the risk of cardiovascular death. 2012 N Engl J Med 366(20):1881-1890)

**Tuesday, May 22, 2012**

**Question:**

What is the natural history of opioid dosage escalation following work related injuries?

**Answer:**

According to a recent study, the percentage of Workers' Compensation claims in which opioids were ever prescribed increased from 43.3% in year 1 to 80.8% in year 7 post-injury. The general message of this article is that opioid dosages tend to escalate as claims mature. (Tao X, et al. Natural history of opioid dosage escalation post-injury. A cohort study of injured workers in the state of Louisiana 2012 J Occ Env Med 54(4):439-444

**Monday, May 21, 2012**

**Question:**

What are the potential adverse effects of amyl nitrite when used as part of a regimen for the treatment of cyanide toxicity?

**Answer:**

The cited reference notes "Amyl nitrite can be associated with potentially serious adverse reactions such as hypotension, syncope, excessive methemoglobinemia, and hemolysis in G6PD deficient patients. These effects are more pronounced in young children, in the elderly, and in patients with cardiac and pulmonary disorders." (Lavon O and Bentur Y. Does amyl nitrite have a role in the management of pre-hospital mass casualty cyanide poisoning? 2010 Clin Tox 48:477-484)

**Friday, May 18, 2012**

**Question:**

The Australian platypus (*Ornithorhynchus anatinus*) is one of only two mammalian species possessing a functional venom delivery apparatus. What is the nature of platypus venom and how is it delivered?

**Answer:**

The first cited reference below notes that venom from the platypus is injected through spurs located on the hind legs that are connected to venom ducts. Interestingly, Only the male platypus possesses this apparatus. Five types of proteins and peptides have been isolated and identified from platypus venom, namely: defensin-like peptides (DLPs); *Ornithorhynchus* venom C-type natriuretic peptides (OvCNPs); *Ornithorhynchus* nerve growth factor; hyaluronidase; and l-to-d-peptide isomerase. (Hodgson WC Pharmacological action of Australian animal venoms. 1997 Clin Exp Pharm Physiol 24:10-17 and Koh JM, et al Platypus venom: source of novel compounds. 2009 Aust J Zoology 57(4):203-210)

**Thursday, May 17, 2012**

**Question:**

QT prolongation and torsades de pointes associated with medications are important issues with regard to the potential toxicity of certain drugs. At the receptor level, what causes drug induced QT prolongation and torsades de pointes?

**Answer:**

QT prolongation and TdP are consequences of inhibition of the rapid component of the delayed rectifier potassium current ( $I_{Kr}$ ), which is conveyed by the human ether-a-go-go-related gene (HERG) potassium channel. (Lin Y, et al. Electrophysiologic, pharmacokinetic and pharmacodynamics values indicating a higher risk of torsades de pointes. 2011 J Clin Pharm 51:819-829)

**Wednesday, May 16, 2012**

**Question:**

What is currently the primary source of lead exposure for U.S. children?

**Answer:**

Contact with deteriorating lead-based paint and lead- contaminated dust and soil is currently the primary source of lead exposure for U.S. children (Campbell C, et al. Primary prevention of lead exposure: The Philadelphia lead safe homes study. 2011 Supplement Public Health Reports 126:76-88)

**Tuesday, May 15, 2012**

**Question:**

Psilocybin is the principal psychoactive component of *Psilocybe* and other genera of mushrooms. At what receptor site are the effects of this psychoactive chemical mediated?

**Answer:**

The effects of psilocybin are primarily mediated at 5-HT<sub>2A</sub> receptor sites. (Griffiths RR, et al. Psilocybin occasioned mystical-type experiences: immediate and persisting dose-related effects. 2011 Psychopharm 218:649-665)

**Monday, May 14, 2012**

**Question:**

What chemical is formed when carbon monoxide comes into contact with nickel? Inhalation of this chemical can be associated with the development of what clinical problem?

**Answer:**

Nickel carbonyl or nickel tetracarbonyl, a colorless, highly volatile and flammable substances forms when carbon monoxide comes into contact with nickel. Inhalation of carbonyl nickel can cause severe chemical pneumonitis that can be fatal. The cited reference points out that nickel carbonyl “may result in toxicity insidiously hours or even days after inhalation of nickel carbonyl vapors. Initial symptoms are usually mild and not specific. These include frontal headache, dizziness, and occasionally nausea and vomiting. Delayed symptoms, such as chest pain, hemoptysis, and cyanosis, have been reported to occur 12 to 24 hours after exposure”. (Raymond CS, et al. Inhalational nickel carbonyl poisoning in waste processing workers. 2005 Chest 128: 424-429)

**Friday, May 11, 2012**

**Question:**

What is CCA pressure treated wood?

**Answer:**

“CCA” stands for chromated copper arsenate. This material is used as a wood preservative and is impregnated, under high pressure, into certain wood products intended for outdoor use to protect the wood from development of fungus, rot and destruction by insects. Chromium, arsenic and copper may become bioavailable specifically when CCA treated woods are burned, cut, or sanded. Under these circumstances (depending on exposure and dose parameters) unprotected exposure to these metals could be clinically important. In 2004, the US EPA banned the use of CCA in wood in residential products including wood used in play structures, decks, picnic tables, landscape timbers, residential fences, patios, walkways and boardwalks. (Decker P, et al. Exposure to wood dust and heavy metals in workers using CCA pressure treated wood. 2002 Am Ind Hyg Assoc J 63:166-171 and Katz SA and Salem H. Chemistry and toxicology of building timbers pressure treated with chromated copper arsenate: a review. 2005 J Applied Tox 25:1-7)

**Thursday, May 10, 2012**

**Question:**

Recent reports have documented phosphine exposure in a number of veterinary workers and veterinarians. How might this group of workers become occupationally exposed to this potentially lethal gas?

**Answer:**

Zinc phosphide (Zn<sub>3</sub>P<sub>2</sub>) is a readily available rodenticide that, on contact with stomach acid and water, produces phosphine (PH<sub>3</sub>), a highly toxic gas. Household pets that ingest Zn<sub>3</sub>P<sub>2</sub> often will regurgitate, releasing PH<sub>3</sub> into the air. Veterinary hospital staff members treating such animals can be poisoned from PH<sub>3</sub> exposure. (Occupational Phosphine Gas Poisoning at Veterinary Hospitals from Dogs that Ingested Zinc Phosphide — Michigan, Iowa, and Washington, 2006–2011. MMWR April 27, 2012 / 61(16):286-288

**Wednesday, May 9, 2012****Question:**

Tularemia is a CDC designated “Category A bioterrorism agent”. In other words, it is considered to be a high-priority organism that poses a risk to national security because: (1) it can be easily disseminated or transmitted from person to person; (2) it may result in high mortality rates and have the potential for major public health impact; (3) it might cause public panic and social disruption; and (4) it may require special action for public health preparedness. What is the causative organism for tularemia and what are the natural reservoirs for this organism in the US?

**Answer:**

According to the cited reference, tularemia is “a zoonotic infection caused by the small, aerobic, pleomorphic Gram negative coccobacillus *Francisella tularensis* to which humans are a highly susceptible host”. The authors also point out that “In the US, rabbits, hares, and ticks are among the most important natural reservoirs for the organism, and infection is most commonly transmitted by tick, deerfly, flea or by direct contact with infected animal products”. While tularemia does have an incidence of natural occurrence in some parts of the US, “a diagnosis of tularemia, in a non-endemic area, should alert the clinician to possible bioterrorism exposure”. (Guffey MB, et al Ulceroglandular tularemia in a nonendemic area. 2007 So Med J 100(3):304-308)

**Tuesday, May 8, 2012****Question:**

Given the fact that carbon monoxide (CO) is approximately 3% lighter than air, what is the optimal location, within a given room, for the placement of residential CO detectors?

**Answer:**

The cited reference reports a study comparing the placement of a CO detector in a model simulating the top, middle and bottom of a room. They determined that CO “did not layer on the floor, did not float at the middle of the chamber (“room”) and did not rise to the top” of the experimental chamber. Rather, these authors demonstrated that the CO infused into their model diffused to create an equal concentration throughout the model. They concluded “it would be reasonable to place a residential CO alarm at any height within a room.” (Hampson N, et al. Should the placement of carbon monoxide (CO) detectors be influenced by CO’s weight relative to air? 2012 J Emerg Med 42(4):478-482)

**Monday, May 7, 2012****Question:**

Which metals, when released from prosthetic implants, have been implicated (but not proven) as causing peripheral neuropathy in some patients?

**Answer:**

Cobalt and vanadium have been implicated (but not proven) as causing peripheral neuropathy in some patients. (Rizzetti MC et al. Loss of sight and sound. Could it be the hip? 2009 The Lancet 373: 1052 and Moretti B et al. peripheral neuropathy after hip replacement failure: is vanadium the culprit? 2012 The Lancet 379:1676)

**Friday, May 4, 2012****Question:**

Patients treated with methotrexate as cancer chemotherapy can develop acute nephrotoxicity since this drug is primarily renally excreted. More prolonged exposure may be associated with suppression of bone marrow function, liver toxicity and oral and GI ulcerations. What are the therapeutic options available to reduce methotrexate toxicity in this setting?

**Answer:**

Leucovorin (folinic acid), in conjunction with aggressive intravenous fluid administration and urine alkalinization, can decrease methotrexate toxicity. In addition, the FDA has recently approved glucarpidase (Voraxaze) to treat elevated plasma levels of methotrexate in these patients. According to the cited reference, glucarpidase is a recombinant bacterial enzyme capable of “converting methotrexate to its inactive metabolites, glutamate and DAMPA, which are metabolized by the liver, providing a non-renal pathway for methotrexate elimination”. (The Medical Letter, March 5, 2012; 54(1385):19-20)

**Thursday, May 3, 2012****Question:**

Dapsone is a sulfone drug often used to prevent the development of *Pneumocystis jirovecii* pneumonia and also in the treatment of leprosy and dermatitis herpetiformis. What important hematologic adverse effects have been associated with the use of this drug?

**Answer:**

Important hematologic adverse effects associated with dapsone use in some patients include the development of Heinz body hemolytic anemia and methemoglobinemia. (Barclay JA et al. Dapsone-induced methemoglobinemia: a primer for clinicians. 2011 Ann Pharmacotherapy 45:1103-1115)

**Wednesday, May 2, 2012****Question:**

What was the Hawk’s Nest Tunnel Disaster?

**Answer:**

The Hawk’s Nest Tunnel was a hydroelectric power project constructed by blasting into massive natural rock formations in the area of Gauley Bridge, West Virginia (undertaken during the 1930’s). When the drilling and blasting phase of the Hawks Nest project was complete, an epidemic of silicosis was identified among men who had worked at the Gauley Bridge site. Four hundred drillers died, and lung-related disabilities were reported in the majority of surviving workers. This has been noted as one of the worst occupational health and public health disasters in the history of the United States. (Greenberg MI, et al Silicosis: a review. 2007 Disease Month 53: 394-416)

**Tuesday, May 1, 2012**



**Question:**

What organochlorine insecticide, with estrogenic properties, was used extensively in the French West Indies to control the banana root borer from the 1970s through the 1990s and resulted in extensive environmental contamination? This chemical has also been associated with an increase in the risk of what cancer?

**Answer:**

Chlordecone (also known as Kepone) is an organochlorine insecticide with well-defined estrogenic properties. It was extensively used from 1973 to 1993 in the French West Indies, to control the banana root borer. An epidemiologic association between exposure to this chemical and the development of prostate cancer in men has been postulated. (Multigner L, et al. Chlordecone exposure and risk of prostate cancer. 2010 J Clin Oncology 28(21): 3457-3462)

**Monday, April 30, 2012**

**Question:**

The anti-helminthic agent levamisole was identified as an adulterant in street cocaine as early as 2003. How widespread is the problem of cocaine adulteration with this potentially dangerous compound?

**Answer:**

By mid 2009, The US Drug Enforcement Administration (DEA) reported that nearly 70% of all cocaine seized by that agency contained levamisole as an adulterant. More recent data has not yet become available. (Agranulocytosis associated with cocaine use. 2009 MMWR 58:1381-1385 as cited in Larocque A and Hoffman RS. Levamisole in cocaine: Unexpected news from an old acquaintance. 2012 Clin Tox 50(4):231-241)

**Friday, April 27, 2012**

**Question:**

How long might the paralysis associated with botulism be expected to persist?

**Answer:**

The cited reference points out "Paralysis from botulism can be long lasting, and is toxin dependent. Mechanical ventilation may be required for 2 to 8 weeks or longer with food borne botulism and paralysis may continue for as long as 7 months. Symptoms of cranial nerve dysfunction and dysautonomia may persist for more than 12 months." (Dembek Z et al. Botulism: Cause, Effects, Diagnosis, Clinical and Laboratory Identification, and Treatment Modalities 2007 Disaster Med Pub Health Preparedness 1:122-134)

**Thursday, April 26, 2012**

**Question:**

While funnel web spiders (Atrax and Hadronyche spp) may be the most deadly of all spiders worldwide, they are generally confined to eastern Australia. What are the clinical characteristics associated with severe envenomation by this group of spiders?

**Answer:**

The authors of the cited reference point out that severe envenomation by funnel web spiders is characterized by "both neuromuscular and autonomic excitation and can be associated with pulmonary edema." They go on to point out that "There is a mixture of catecholaminergic and cholinergic excess with bradycardia or tachycardia, hypertension, miosis or mydriasis, hypersalivation, lacrimation, diaphoresis and piloerection." In addition, the authors state "Neuromuscular excitation manifests as paresthesias, fasciculations (typically involving the tongue) and muscle spasms." They emphasize that "non-specific symptoms such as vomiting, headache, and fatigue occur and patients can be irritable or agitated." (Isbister GK and Fan HW. Spider bite. 2011 The Lancet 378:2039-2047)

**Wednesday, April 25, 2012**

**Question:**

The jequirity bean (Abrus precatorius) also known as the rosary pea, prayer bead, Buddhist rosary bead, crabs eye, weather plant or lucky bean can be lethal if ingested. What is the toxin at issue that may be emanated from this plant and what are the clinical characteristics associated with poisoning involving this toxin?

**Answer:**

The toxin at issue is abrin. The cited reference points out "Patients usually present with nausea, vomiting, diarrhea, abdominal cramps, hematemesis and melena, which occur due to the irritant effects of abrin on the gastrointestinal mucosa. Acute renal failure may occur due to hemagglutination, hemolysis of red cells, hypovolaemic shock and a direct toxic effect on the kidneys. Hepatotoxicity may occur leading to elevated levels of transaminases and serum bilirubin. Drowsiness and convulsions may also occur and contact with the eyes may cause irritation and blindness, and skin contact may result in a rash". (Fernando C. Poisoning due to Abrus precatorius (jequirity bean), 2001 Anesthesia 56:1178-1180)

**Tuesday, April 24, 2012**

**Question:**

The perforation of colonic diverticula is a serious complication of diverticular disease and may even result in death in some cases. What drugs have been posited to be associated with an increased risk of colonic diverticular perforation and what are the possible mechanisms associated with this phenomenon?

**Answer:**

The cited reference notes an increased rate of diverticular perforation associated with NSAIDs and corticosteroids. It is proposed that "these drugs may interfere with the mucosal barrier function in the bowel". In addition, opioids may increase colonic transit time and raise the intraluminal pressure thus increasing the risk for colonic diverticular perforation. (Piekarek K and Israelsson LA. Perforated colonic diverticular disease: the importance of NSAIDs, opioids, corticosteroids, and calcium channel blockers. 2008 Int J Colorectal Dis 23:1193-1197)

**Monday, April 23, 2012**

**Question:**

Prior to the beginning of the age of chemotherapy in the 1950s, the only recognized cause of so-called hepatic veno-occlusive disease (VOD) was the ingestion of herbal teas or foods containing pyrrolizidine alkaloids. What plants contain these alkaloids?

**Answer:**

The cited reference notes that plants containing pyrrolizidine alkaloids capable of causing hepatic veno-occlusive disease include Crotalaria spp, Heliotropium spp, Senecio spp, and, less frequently, Symphytum [comfrey]. (DeLeve LD et al. Toxic Injury to Hepatic Sinusoids: Sinusoidal Obstruction Syndrome (Veno-Occlusive Disease). 2002 Seminars in Liver Disease 22(1):27-41)

**Thursday, April 19, 2012**

**Question:**

The use of metal-on-metal hip implants has become common worldwide. Post-implant procedure, however, blood levels of metal ions are usually elevated. Which metal ions are most commonly involved? In which groups of patients may metal-on-metal implants be contraindicated due to the liberation of metal ions?

**Answer:**

The cited reference notes "All patients with metal-on-metal hip implants have a permanently raised level of chrome and cobalt metal ions in their blood". They go on to report "The use of the metal-on-metal bearing may be contraindicated in patients with renal insufficiency (because these ions are excreted by the kidney) and in women of child-bearing age for the fully justifiable argument of placental passage of these ions." (Triclot P. Metal-on-metal: history, state of the art. 2011 International Ortho 35:201-206)

**Wednesday, April 18, 2012**

**Question:**

With regard to accidental caustic ingestions in pediatric patients, what is the best predictor of morbidity and mortality?

**Answer:**

The extent of injury at initial evaluation remains the best predictor of morbidity and mortality in pediatric patients following an accidental caustic ingestion. (Kay M and Wyllie R. Caustic ingestions in children. 2009 Curr Opinion in Pediatrics 21:651-654)

**Tuesday, April 17, 2012**

**Question:**

What is silo filler's disease?

**Answer:**

Silo-filler's disease is an occupational disease associated with exposure to ensiled crops (crops in a silo) and the production of oxides of nitrogen within the silage. Studies have confirmed that high levels of NO, NO(2), and N(2)O(4) are often produced in silos. These gases are dense and tend to settle in the chute and around the base of the silo, and exposure may occur without anyone's entering the silo.

Although NO(2) is brown and has an odor, N(2)O(4) is colorless and odorless, and exposure can occur without warning. If undetected by smell or sight, the potent nitrogen oxides may be inhaled deep into the lungs, where contact with the mucosal moisture produces nitric acid, which burns the airways, respiratory bronchioles, and alveoli. In fatal exposures, vascular collapse and the outpouring of serum rapidly produce shock and death. In another clinical course associated with silo-filler's disease, exposure causes cough and chest tightness. Although these conditions clear spontaneously, illness may return within one month with severe symptoms of fever, chills, and shortness of breath. Biopsies show a bronchiolitis obliterans with granuloma formation. This second pattern may respond to steroids. (MMWR. Epidemiologic Notes and Reports Silo-Filler's Disease in Rural New York. July 23,1982; 31(28):389-391)

**Monday, April 16, 2012**

**Question:**

What is the basis for the so-called "Antabuse reaction"?

**Answer:**

Antabuse (disulfiram) inhibits the enzyme aldehyde dehydrogenase. This is the enzyme that metabolizes acetaldehyde; a product of the metabolism of ethanol mediated by the enzyme alcohol dehydrogenase. Drinking ethanol while taking disulfiram thus causes acetaldehyde to accumulate. This accumulation of acetaldehyde results in a variety of symptoms including headache, nausea, palpitations, and facial flushing. (Ehrlich RI et al. Disulfiram reaction in an artist exposed to solvents. 2012 Occupational Medicine 62:64-66)

**Friday, April 13, 2012**

**Question:**

How common is medication-induced pancreatitis in pediatric patients?

**Answer:**

According to the cited reference, most studies attribute pediatric pancreatitis to medications in less than 25% of cases. The authors indicate "the most common medications implicated are valproic acid, L-asparaginase, prednisone, and 6-mercaptopurine and go on to report "No clear mechanism has been delineated for the development of medication-induced pancreatitis. Interpretation of the cause-and-effect relation between drugs and pancreatitis is difficult and must be approached cautiously. For instance, many patients on prednisone have systemic illnesses that, in and of themselves, may predispose to pancreatitis." (Bai HX et al. What have we learned about acute pancreatitis in children? 2011 J Ped Gastro and Nutrition 52(3):262-270)

**Thursday, April 12, 2012**

**Question:**

What is Yperite?

**Answer:**

Yperite is a somewhat archaic (but still used) word for the chemical warfare agent sulfur mustard. (Cojocar B, et al. Sensitizers on inorganic carriers for decomposition of the chemical warfare agent yperite. 2008 Environ Sci Technol 42: 4908-4913)

**Wednesday, April 11, 2012**

**Question:**

Hydrofluoric acid (HF) is widely used in the oil refining industry. In fact, some of the most severe HF disasters have historically taken place at refinery sites. Why is HF so widely used in the oil refining industry?

**Answer:**

HF is used as an alkylation catalyst in the manufacture of high-octane fuels. Approximately 30% of the nations roughly 150 refineries use this chemical on site. (Johnson J. Hydrofluoric acid safety. 2012 Chemical and Engineering News 90(14):21)

**Tuesday, April 10, 2012**

**Question:**

In 2008, an outbreak of selenium poisoning was reported in 201 individuals in 10 states. These people consumed a liquid dietary supplement containing 200 times the labeled concentration of selenium; median estimated dose of selenium was 41,749 microgram per day (recommended dietary allowance for selenium is 55 microgram per day). What were the most frequently reported symptoms associated with this outbreak?

**Answer:**

The most frequently reported symptoms associated with this outbreak included diarrhea (78%), fatigue (75%), hair loss (72%), joint pain (70%), nail discoloration or brittleness (61%), and nausea (58%). Symptoms persisting 90 days or longer included fingernail discoloration and loss (52%), fatigue (35%), and hair loss (29%). (MacFarquhar JK et al. Acute selenium toxicity associated with a dietary supplement. 2010 Arch Int Med 170(3):256-261)

**Monday, April 9, 2012**

**Question:**

A 25-year-old male presents to the emergency department with skeletal muscle weakness and severe respiratory distress as well as severe hypokalemia and rhabdomyolysis after the intentional ingestion of a depilatory (hair removal product). What chemical constituent of this product is likely responsible for the clinical findings in this case?

**Answer:**

The most likely component of the depilatory causing the clinical manifestations in this case is barium sulfate. (Sigue G, et al. From profound hypokalemia to life-threatening hyperkalemia: a case of barium sulfate poisoning. 2000 Arch Int Med 160:548-551)

**Friday, April 6, 2012**

**Question:**

Millions of persons are exposed to arsenic concentrations > 10 µg/L in drinking water in the US. In Bangladesh, China, India, Cambodia, Ghana, Argentina, Mexico, and other countries around the world, populations are exposed to arsenic levels in drinking water well in excess of 10 µg/L. Environmental exposure to arsenic has been posited to be associated with hypertension in persons living in arsenic-endemic areas. What evidence exists to support this notion?

**Answer:**

A recent systematic review identified an association (but not causation) between arsenic and the prevalence of hypertension. The authors point out "Additional evidence is needed to evaluate the dose-response relationship between environmental arsenic exposure and hypertension." (Abhyankar LN, et al. Arsenic exposure and hypertension: A systematic review. 2012 Environ Health Perspect 120:494-500)

**Thursday, April 5, 2012**

**Question:**

Recent reports document skin rashes in children secondary to contact with caterpillars. What is the pathologic mechanism for these rashes?

**Answer:**

The pathologic mechanism for rashes from skin contact with caterpillars is not fully understood and is somewhat dependent on the specific species of caterpillar. However, the mechanism is thought to involve exposure to chemicals on caterpillar or cocoon hairs (spicules) or to mechanical irritation from these structures. The cited reference points out that when caterpillars and cocoons are in high density, particularly susceptible persons may develop a rash if these structures become airborne. (MMWR March 30,2012, 61(12):209-211)

**Wednesday, April 4, 2012**

**Question:**

Toxic epidermal necrolysis (TEN) is a life-threatening exfoliative skin disease involving skin blistering and extensive skin shedding. This disorder is often associated with the administration of a variety of drugs with up to 95% of cases being deemed drug-related. What is the clinical presentation for drug-induced TEN?

**Answer:**

According to the cited reference, "Drug-induced TEN typically presents with fever and influenza-like symptoms 1 to 3 wks after the application of the suspected drug . One to 3 days later, signs begin in the mucous membranes, including eyes, mouth, nose, and genitalia in up to 90% of cases. Skin lesions manifest as generalized macules with purpuric centers. The macules progress to large confluent blisters with subsequent epidermal detachment, yet never show involvement of the hair. In the following 3 to 5 days, separation of the epidermis progresses and leads to large denuded areas. The large wound area leads to extreme pain, massive loss of fluid and protein, bleeding, evaporative heat loss with subsequent hypothermia, and infection. (Gerull R, et al. Toxic epidermal necrolysis and Stevens-Johnson syndrome: A review. 2011 Crit Care Med 39:1521-1532)

**Tuesday, April 3, 2012**

**Question:**

Priapism is a persistent penile erection that continues hours beyond, or is unrelated to, sexual stimulation. In some cases priapism can be precipitated by a variety of drugs and medications. What drugs and medications have been associated with priapism?

**Answer:**

The drugs and medications that have been associated with priapism include: antihypertensives, anticoagulants, antidepressants, alcohol, marijuana, cocaine and vasoactive drugs used for intracavernous injection therapy including alprostadil, papverine, prostaglandin E1 and phentolamine (as well as others). (Priapism: Guideline on the management of priapism. 2003 American Urological Association. Available at <http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines.cfm>)

**Monday, April 2, 2012**

**Question:**

If nitrous oxide comes into contact with certain chemicals a violent reaction may ensue. What are those chemicals?

**Answer:**

Contact of nitrous oxide with aluminum, boron, hydrazine, lithium hydride, phenyllithium, phosphine, sodium, tungsten carbide, hydrogen, hydrogen sulfide, organic peroxides, ammonia, or carbon monoxide may cause violent reactions to occur. (<http://www.osha.gov/SLTC/healthguidelines/nitrousoxide/recognition.html>)

**Friday, March 30, 2012**

**Question:**

An occupational disorder known as acro-osteolysis was first described in 1950 in a blacksmith. What is acro-osteolysis? Exposure to what chemical has been causally associated with this disorder?

**Answer:**

Occupationally derived acro-osteolysis is a reversible disorder characterized by bony destructive lesions of the distal phalanges of one or more fingers (most frequently involving the thumbs). Acro-osteolysis has been recognized in a very small percentage of workers (less than 2%) involved with the polymerization of vinyl chloride. (Gama C, et al. Occupational acro-osteolysis. 1978 J Bone Joint Surg 60-A(1):86-90)

**Thursday, March 29, 2012**

**Question:**

What is the definition for the CDC Category A Agent bioterrorism agent? What are the currently listed Category A Agents?

**Answer:**

The CDC defines category A Agents as follows: "The U.S. public health system and primary healthcare providers must be prepared to address various biological agents, including pathogens that are rarely seen in the United States. High-priority agents include organisms that pose a risk to national security because they 1-can be easily disseminated or transmitted from person to person; 2-result in high mortality rates and have the potential for major public health impact; 3-might cause public panic and social disruption; and 4-require special action for public health preparedness".

Category A agents include: 1- Anthrax (*Bacillus anthracis*); 2-Botulism (*Clostridium botulinum* toxin); 3-Plague (*Yersinia pestis*); 4-Smallpox (*variola major*); 4-Tularemia (*Francisella tularensis*; 5-Viral hemorrhagic fevers (filoviruses [e.g., Ebola, Marburg] and arenaviruses [e.g., Lassa, Machupo]) ( <http://emergency.cdc.gov/agent/agentlist-category.asp>)

**Wednesday, March 28, 2012**

**Question:**

What is a "dirty bomb"?

**Answer:**

A dirty bomb is a mix of explosives, such as dynamite, with radioactive powder or pellets. When the dynamite or other explosives are set off, the blast carries radioactive material into the surrounding area. The main danger from a dirty bomb is from the explosion, which can cause serious injuries and property damage. The radioactive materials used in a dirty bomb would probably not create enough radiation exposure to cause immediate serious illness, except to those people who are very close to the blast site. However, the radioactive dust and smoke spread farther away could be dangerous to health if it is inhaled. (<http://emergency.cdc.gov/radiation/dirtybombs.asp>)

**Tuesday, March 27, 2012**

**Question:**

Hydrogen sulfide is a flammable, colorless gas with a characteristic odor of rotten eggs. Hydrogen sulfide may be found associated with a number of industrial activities, such as food processing, coke ovens, paper mills, tanneries, and petroleum refineries. It also occurs naturally in a variety of settings; what are they?

**Answer:**

Hydrogen sulfide (H<sub>2</sub>S) occurs naturally in crude petroleum, natural gas, volcanic gases, and hot springs. It can also result from bacterial breakdown of organic matter. It is also produced by human and animal wastes. (ATSDR, Toxic Substances Portal, available at <http://www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=67>)

**Monday, March 26, 2012**

**Question:**

Does oral calcium supplementation alter the risk for lead toxicity in children?

**Answer:**

According to one recent study of Nigerian children, aged 12-18 months, (mean baseline blood lead levels of 11.1 micrograms per deciliter) who received oral calcium supplementation, calcium supplementation did not affect blood lead levels. However, it is important to understand that other studies have shown opposite results. Thus, it has not yet been definitively proven if calcium supplementation does or does not alter the risk for lead toxicity in young children. (Keating EM et al. The effect of calcium supplementation on blood lead levels in Nigerian children. 2011 J Pediatr 159:845-850)

**Friday, March 23, 2012**

**Question:**

Gender-specific issues have often not been effectively included into most exposure assessment paradigms. Many studies fail to account for the effects of gender specific differences with regard to such factors as pulmonary particle deposition, smoking behaviors, nutritional status, immune factors, and hormonal effects. One very important gender specific factor is the gender variation in the use of personal protective equipment (PPE), specifically respiratory protective equipment. What is the basis for the gender differences with regard to respiratory PPE?

**Answer:**

The basis for the gender differences with regard to respiratory PPE involves the fact that in general respirator masks have been found to fit females more poorly than males and females. In addition females are less likely to receive appropriate training in the use of such PPE as a result of employment patterns that find females fulfilling part time/temporary employment more commonly than males. (Muzaffar S and Christiani DC. Frontiers in occupational and environmental lung disease research. 2012 Chest 141(3):772-781)

**Thursday, March 22, 2012**

**Question:**

What is the reported incidence of drug diversion among health care professionals?

**Answer:**

The reported incidence of drug diversion among health care professionals is reported to be in the range of 1%-2%. However estimates based on anonymous self-reporting imply that the incidence of drug diversion among health care professionals may be as high as 10%. (Hamza H and Bryson EO. Buprenorphine maintenance therapy in opioid-addicted health care professionals returning to clinical practice: A hidden controversy. 2012 Mayo Clin Proc 87(3):260-267)

**Wednesday, March 21, 2012**

**Question:**

What is the difference in chemical structure and pharmacologic action between methylnaltrexone (trade name Relistor) and the drugs naloxone and naltrexone?

**Answer:**

Methylnaltrexone is a peripheral opioid antagonist that is approved for use in the treatment of opioid-induced constipation in patients who are receiving opioids as part of a palliative care regimen. It is a positively charged quarternary ammonium compound and it is this positive charge that limits its ability to traverse the blood-brain barrier. Thus, unlike the tertiary opioid antagonists naloxone and naltrexone, methylnaltrexone does not reverse central mediated analgesia or induce withdrawal. (Sawh SB et al. Use of methylnaltrexone for the treatment of opioid-induced constipation in critical care patients. 2012 Mayo Clin Proc 87(3):255-259)

**Tuesday, March 20, 2012**

**Question:**

What chemical weapon has been said to have the odor of geraniums and has been called the “dew of death”?

**Answer:**

The arsenical compound lewisite has been said to have the odor of geraniums and has been called the “dew of death. (Vilensky JA. “Dew of Death: the story of lewisite, Americas World War I weapon of mass destruction” 2005 Indiana University Press)

**Monday, March 19, 2012**

**Question:**

What is epigenetics?

**Answer:**

Regarding the concept of epigenetics, the cited reference notes that “First introduced by C.H. Waddington in 1939 to name “the causal interactions between genes and their products, which bring the phenotype into being,” epigenetics was later defined as heritable changes in gene expression that are not due to any alteration in the DNA sequence.” (Waddington CH. Preliminary notes on the development of the wings in normal and mutant strains of drosophila. 1939 Proc Natl Acad Sci U S A, 25:299-307 and Holliday R. The inheritance of epigenetic defects. 1987 Science, 238:163-170, as cited in Esteller M. Epigenetics and cancer. 2008 NEJM 358:1148-1159)

**Friday, March 16, 2012**

**Question:**

Over the past 60 years, large amounts of perchlorates have been released in the western United States, often in association with defense-related activities. What defense related activities may be associated with increased levels of perchlorates in ground water?

**Answer:**

The cited reference discusses the fact that the ammonium and potassium salts of perchlorate are used in solid rocket propellants as well as in munitions, explosives, and pyrotechnics, (they are also found in association with road flares, automobile air-bag systems, and various other commercial processes and products). The authors specifically point out “Large volumes of perchlorate-containing wastes have been locally released into the environment, and the solubility of the salts and non-reactivity of ClO<sub>4</sub><sup>-</sup> lead to a highly mobile contaminant that readily migrates to ground- and surface waters.” (Parker DR, et al. Perchlorate in ground water: A synoptic survey of “pristine” sites in the coterminous United States. 2008 Env Sci Technol 42: 1465–1471)

**Thursday, March 15, 2012**

**Question:**

Amiodarone is an antiarrhythmic drug that may be useful for both atrial and ventricular arrhythmias. It exhibits a combination of calcium channel blockade, beta blockade and class III antiarrhythmic effects. Amiodarone has been associated with multiple potentially serious systemic adverse effects; what are they?

**Answer:**

Amiodarone has been associated with bradycardia, hypo- or hyperthyroidism, pulmonary toxicity, ocular deposits, and abnormalities of hepatic function. (Doyle JF et al. Benefits and risks of long-term amiodarone therapy for persistent atrial fibrillation: A meta-analysis. 2009 Mayo Clin Proc.84(3):234-242)

**Wednesday, March 14, 2012**

**Question:**

Respiratory problems related to nitrogen dioxide exposure in indoor ice hockey rinks have occasionally been reported. What is the source for nitrogen dioxide in ice rinks and how do high levels of this gas build to dangerous levels in these settings?

**Answer:**

The cited reference notes that respiratory illness related to nitrogen dioxide exposure in indoor ice arenas has been reported. The authors note that hazardous levels of nitrogen dioxide in ice arenas may be due to malfunction of propane-fueled ice resurfacing equipment in conjunction with poor arena ventilation. Most ice rinks are designed to minimize natural ventilation in order to keep warm air away from the ice surface. This can create a thermal inversion in which cold air and gases (especially nitrogen dioxide- which is denser than air) become trapped close to the ice. The protective glass between spectator stands and the ice rink creates an additional barrier to airflow. (MMWR March 2,2012, 61(8):139-142)

**Tuesday, March 13, 2012**

**Question:**

What are the risk factors for the development of statin-associated myopathy?

**Answer:**

The risk factors for the development of statin-associated myopathy include: concurrent medications ( eg fibrates and calcium channel blockers), older age, hypothyroidism, hepatic dysfunction, and a high body mass index. (David WS. Case 7-2012: A 79 year old man with pain and weakness in the legs. 2012 NEJM 366(10):944-954)

**Monday, March 12, 2012**

**Question:**

How is "severe myotoxicity" associated with statin drugs defined and what is the incidence of "severe" myotoxicity in this setting?

**Answer:**

Severe myotoxicity due to statins is defined as a creatine kinase level exceeding 10 times the upper limit of the normal range, associated with muscle symptoms requiring hospital admission. The incidence of "severe" myotoxicity due to statins is estimated to be 0.1 to 1.0% or 0.4 to 1.1 per 10,000 patient-years. (David WS, et al. Case 7-2012: A 79 year old man with pain and weakness in the legs. 2012 NEJM 366(10):944-954)

**Friday, March 9, 2012**

**Question:**

Primary hyperparathyroidism in patients receiving chronic lithium therapy is common with an absolute risk of 10% versus 0.1% in the general population. What is the likely mechanism for lithium- associated hyperparathyroidism?

**Answer:**

The cited reference notes that the likely mechanism for lithium-associated hyperparathyroidism involves "lithium's inactivation of the calcium-sensing receptor and interference with intracellular second messenger signaling". This leads to an increased release of parathyroid hormone, which increases blood calcium concentrations. (Szalat A. et al. Lithium associated hyperparathyroidism: report of four cases and review of the literature. 2009 Eur J Endocrinol 160:317-323 as cited in McKnight RF et al. Lithium toxicity profile: a systematic review and meta-analysis. 2012 Lancet 379:721-728)

**Thursday, March 8, 2012**

**Question:**

What is litargirio?

**Answer:**

Litargirio (also known as litharge or lead monoxide) is a yellow or peach-colored powder used as an antiperspirant/deodorant and a folk remedy in some segments of the Hispanic community. Lead monoxide (litargirio) is used in the legitimate manufacture of batteries, glass, and ceramics; in the vulcanizing of rubber; and as a paint pigment. Dominicans, particularly those from rural areas, sometimes use litargirio as an antiperspirant/deodorant and as a traditional remedy for burns and fungal infections of the feet. It has been identified as a potential source of lead exposure for some Hispanic children in the U.S.A. (MMWR, Lead poisoning associated with use of litargirio. March 11,2005, 54(9):227-229)

**Wednesday, March 7, 2012**

**Question:**

What was the so-called "toxic oil syndrome" (TOS)? When and where did the primary outbreak of this disorder occur and what were the clinical manifestations of this disorder?

**Answer:**

The cited reference reports that "In 1981, in Spain, the ingestion of an oil fraudulently sold as olive oil caused an outbreak of a previously unrecorded condition, later known as toxic oil syndrome (TOS), clinically characterized by intense incapacitating myalgias, marked peripheral eosinophilia, and pulmonary infiltrates. Of the 20,000 persons affected, approximately 300 died shortly after the onset of the disease and a larger number developed chronic disease." (Gelpi E. et al. The Spanish toxic oil syndrome 20 years after its onset: A multidisciplinary review of scientific knowledge. 2002 Env Health Persp 110(5): 457-464)

**Tuesday, March 6, 2012**

**Question:**

There have been 12 methylene chloride related deaths associated with professional bathtub refinishing operations during the years 2000–2011. What makes this profession especially vulnerable to the adverse effects of methylene chloride?

**Answer:**

Methylene chloride is a highly volatile, colorless, potentially dangerous chemical that is widely used as a degreaser, process catalyst, and paint remover. Bathtub refinishers frequently use stripper compounds that contain this chemical. They often work in poorly ventilated small bathrooms and often do not wear appropriate respiratory protective gear. In addition, methylene chloride vapors are heavier than air and they likely remain in the bathtub after application. Further, the 1997 OSHA standard for methylene chloride requires air monitoring, medical surveillance, hazard communication, and personal protective equipment be in place where methylene chloride is used. The bathtub refinishing industry, in some cases, has fallen behind in maintaining this standard. (MMWR February 24,2012, 61(07):119-122)

**Monday, March 5, 2012**

**Question:**

A new, oral spray formulation of zolpidem (Ambien), has recently been approved for the treatment of short term insomnia characterized by difficulty falling asleep. What are the reasons that this formulation may be more readily used to excess when compared with the tablet form of the drug?

**Answer:**

It is feared that because this new oral spray form of zolpidem has a sweet taste, delivers a relatively high concentration (50mg/mL) of drug and is extremely easy to use, that overuse may become more common than with the tablet form of the drug. (The Medical Letter February 20,2012, 54(1384): 14-15)

**Friday, March 2, 2012**

**Question:**

So called “asthma cigarettes” were marketed in the U.S. in the 1800’s and early 1900’s. What were these cigarettes made from and what was their mechanism of action with regard to asthma treatment?

**Answer:**

Asthma cigarettes of the 19th and early 20th Centuries were made from the leaves of the *Datura stramonium* plant. These cigarettes provided an inhalational dose of antimuscarinic alkaloid. This was, in essence, the forerunner of certain current asthma medications including ipratropium bromide and tiotropium bromide. (Mutius E and Drazen JM. A patient with asthma seeks medical advice in 1828, 1928 and 2012. 2012 NEJM 366:827-834)

**Thursday, March 1, 2012**

**Question:**

What is the main source of environmental dioxins in the United States today?

**Answer:**

According to the U.S. Environmental Protection Agency (EPA), the open-air burning of backyard waste is currently the main source of dioxins in the United States. (Hogue C. Dioxins, assessed at last. February 27,2012, Chemical & Engineering News- digital edition)

**Wednesday, February 29, 2012**

**Question:**

For individuals who have habitually smoked cigarettes since their early adult years, what is their estimated reduction in life expectancy?

**Answer:**

According to the cited reference “Those who have habitually smoked cigarettes since early adult life but stopped at 60, 50, 40 or 30 years of age gain, respectively, about 3, 6, 9 or (approximately) 10 years of life expectancy in comparison with those who continue to smoke”. (International Agency for Research on Cancer, 2007 World Health Organization, volume 11 “Reversal of Risk After Quitting Smoking”; page 15)

**Tuesday, February 28, 2012**

**Question:**

Kapchunka has been implicated as the cause for botulism in the U.S. in a few isolated cases over the years. What is kapchunka and what serotype of botulism was caused by kapchunka?

**Answer:**

Kapchunka is ungutted, dried, salted whitefish product that is not cooked before eating. Serotype E botulism has been identified in conjunction with kapchunka. (MMWR September 6,1985 34(35):546-547)

**Monday, February 27, 2012**

**Question:**

The bite of the brown recluse spider (genus *Loxosceles*) causes a condition known as loxoscelism. The hallmark of this condition involves dermal necrosis. What is the pathogenesis of loxoscelism?

**Answer:**

The cited reference notes that the exact pathways of action for *Loxosceles* venom have not yet been fully elucidated. However the author points out that key components of phospholipase D participate in the development of dermal necrosis. The author goes on to point out that “injection of venom triggers a complex inflammatory response, including the release of pro-inflammatory cytokines and lipid mediators. Additionally, the venom has a direct hemolytic effect on red blood cells, can cause complement activation and platelet aggregation, and contains an hyaluronidase that increases the size of the tissue lesion, which is a hallmark of loxoscelism.” (Isbister GK. Spider bite. 2011 The Lancet 378:2039-2047)

**Friday, February 24, 2012**

**Question:**

For patients in status epilepticus, which is safer and more effective for pre-hospital treatment; IM midazolam or IV lorazepam ?

**Answer:**

A recently reported double-blind, randomized, noninferiority trial concluded “For subjects in status epilepticus, intramuscular midazolam is at least as safe and effective as intravenous lorazepam for prehospital seizure cessation.” (Silbergleit R. et al Intramuscular versus Intravenous Therapy for Prehospital Status Epilepticus. 2011 NEJM 366:591-600)

**Thursday, February 23, 2012**

**Question:**

What were the peak years of maximum leaded gasoline usage in the United States?

**Answer:**

The peak years of leaded gasoline usage in the United States were 1960 through 1975. (Robbins N, et al. Childhood lead exposure and uptake in teeth in the Cleveland area during the era of leaded gasoline. 2010 Sci Tot Env 408:4118-4127)

**Wednesday, February 22, 2012**

**Question:**

What is the incidence of peripheral edema associated with the therapeutic use of calcium channel blockers (CCBs) and what is the most likely mechanism?

**Answer:**

Peripheral edema is a common (reported incidence ranging from 1.8% to as high as 33% of patients) and troublesome adverse effect of CCBs. It is theorized to result from arteriolar dilatation causing intra-capillary hypertension with local extravasation of fluid. (Makani H, et al. Peripheral edema associated with calcium channel blockers: incidence and withdrawal rate – a meta-analysis of randomized trials. 2011 J Hypertension 29:1270-1280)

**Tuesday, February 21, 2012****Question:**

What is “crack eye” and what are the proposed causes for this problem?

**Answer:**

“Crack eye” refers to corneal injury associated with the use of crack cocaine. The smoke emanating from crack cocaine may be directly damaging to the corneal epithelium that may be enhanced by the anesthetic properties of cocaine that can result in a decreased blink rate. The cited reference points out “devitalization of the corneal nerves decreases the corneal epithelial integrity, leading to neurotrophic keratopathy”. In addition, cocaine smoke can be very irritating and thus users may repeatedly rub their eyes causing infectious complications often due to *Staphylococcus aureus* and streptococcal species. Fungal infections have been implicated in some cases. (Miller AD and Sherman SC. Crack eye. 2009 J Emerg Med, 37(1):75–76)

**Monday, February 20, 2012****Question:**

What is the Kounis syndrome?

**Answer:**

Kounis syndrome is the concurrence of acute coronary syndrome with an acute allergic reaction. The pathophysiologic characteristics of Kounis syndrome involve coronary artery spasm and/or atheromatous plaque erosion or rupture during an allergic reaction resulting in acute coronary syndrome and/or myocardial infarction. Allergic reactions to a large number of medications have been implicated in the development of Kounis syndrome. (Lopez PR and Peiris AN. Kounis syndrome. Southern Med J 2010 103(11):1148-1155)

**Friday, February 17, 2012****Question:**

Visual effects, especially bluish discoloration of vision, have been reported (albeit rarely) in conjunction with which widely prescribed medications?

**Answer:**

Visual effects, especially bluish discoloration of vision, have been reported (albeit rarely) in conjunction with the use of the three currently available phosphodiesterase 5 inhibitors: sildenafil (Viagra), tadalafil (Cialis), and vardenafil (Levitra). (The Medical Letter, February 6, 2012; 54(1383):10-11)

**Thursday, February 16, 2012****Question:**

Inhalation (snorting) of cocaine (powder) has been associated with the development of a variety of oro-nasal problems. What are they?

**Answer:**

Inhalation (snorting) of cocaine (powder) has been associated with the development of epistaxis, chronic rhinitis, nasal septal perforation, destruction of the lateral nasal walls leading to the saddle nose deformity and palatal necrosis. (Goodger NM et al. Palatal and nasal necrosis resulting from cocaine misuse. 2005 Br Dental J 198(6):333-334) and (Messinger E. Narcotic septal perforations due to drug addiction. 1962 J Am Med Assoc 1962; 179: 964)

**Wednesday, February 15, 2012****Question:**

Occupational exposure to what substance has been reported to be associated with the development of a greenish discoloration of the tongue?

**Answer:**

Occupational exposure to vanadium and vanadium containing compounds has been reported to be associated with the development of a greenish discoloration of the tongue. (Venkataraman BV and Sudha S. Vanadium Toxicity 2005 Asian J Exp Sci 19(2):127-134)

**Tuesday, February 14, 2012****Question:**

What is the principal etiological factor in causing the demyelinating condition known as central pontine myelinolysis (CPM)?

**Answer:**

The principal etiological factor in causing central pontine myelinolysis (CPM) is the rapid correction of hyponatremia. It is hypothesized that overly rapid correction of hyponatremia results in osmotic stress. The cited reference points out that CPM “often occurs on a background of chronic systemic illness, and is commonly observed in individuals with alcoholism, malnutrition and liver disease”. (Norenberg MD. Central pontine myelinolysis: historical and mechanistic considerations. 2010 Metab Brain Dis 25:97–106)

**Monday, February 13, 2012****Question:**

What genus of sea snake has been reported to be the only sea snake to inhabit US waters?

**Answer:**

The range of the yellow-bellied sea snake, *Pelamis platurus*, in terms of square miles inhabited, exceeds that of any other genus of snakes in the world as this snake is not confined to coastal waters but extends far into the open ocean. *Pelamis platurus* is the only genus of sea snake ever to be identified in US waters and has been reported in coastal waters of southern California. (Hecht MK, et al. Distribution of the yellow bellied sea snake, *Pelamis platurus*, and its significance in relation to the fossil record. 1974 Herpetologica 30(4):387-396)



**Friday, February 10, 2012**

**Question:**

In 1997, 48-year-old chemistry professor Karen Wetterhahn died as a result of a minimal skin (with or without concomitant possible inhalational) exposure to what mercury-containing compound often said to be “supertoxic”?

**Answer:**

Several months following an inadvertent laboratory accident, Dr. Wetterhahn succumbed to mercury toxicity following exposure to a very small amount of dimethylmercury. (Nierenberg DW et al. Delayed cerebellar disease and death after accidental exposure to dimethylmercury. 1998 NEJM 338(23):1672-1676)

**Thursday, February 9, 2012**

**Question:**

Drug induced systemic lupus erythematosus is defined as a lupus syndrome that is related on a temporal basis to continuous drug exposure occurring in patients with no prior history of lupus and resolving after discontinuation of the offending drug. (Hess, 1988) When was drug-induced lupus first described and what drug was the first drug noted as causative of this disorder?

**Answer:**

Drug-induced systemic lupus erythematosus was first reported in 1945 in association with sulfadiazine. (Marzano AV et al. Drug-induced subacute cutaneous lupus erythematosus: evidence for differences from its idiopathic counterpart. 2011 Brit J Derm 165:335-341) and (Hess E. Drug-related lupus. 1980 NEJM 318:1460-1462)

**Wednesday, February 8, 2012**

**Question:**

Over time, many instances of perceived toxicological illness have proven to involve the phenomenon of “mass hysteria”. What is “mass hysteria”?

**Answer:**

According to the cited reference, mass hysteria involves “the rapid development of heightened fear and anxiety, which then translates into massive disruption to the behavior and activities of those involved”. Another source (Pastel, 2001) reports: “Most epidemics of mass hysteria are initiated by an actual event, but some can originate from mere rumors of a catastrophic situation. In cases associated with water contamination, smog, nuclear accidents, or chemical exposure, a common trigger is an odor, or perception of an odor. The outbreak may then be perpetuated by a variety of factors such as physical or visual proximity to casualties, general excitement of the event, presence of media at the event, litigation and/or compensation cases, labeling the phenomenon with a specific illness diagnosis, and persistence of rumors.” (Balaratnasingam S and Janca A. Mass hysteria revisited. 2006 Curr Opin Psychiatry 19:171-174 and Pastel RH. Collective behaviors: Mass panic and outbreaks of multiple unexplained symptoms. 2001 Mil Med 166:44–46)

**Tuesday, February 7, 2012**

**Question:**

Nonlethal doses of camphor have been reported to result in hallucinations, tremors, syncope, arrhythmias, seizures, and abortion. Chronic ingestion of camphor may result in hepatotoxicity. What is the concentration of camphor that is routinely found in over the counter products that contain this potentially dangerous substance?

**Answer:**

The cited reference notes that in 1983 the sale of products containing greater than 11% camphor was discontinued. Nonetheless products containing 11% camphor, as well as lower concentrations, remain the cause of serious poisonings involving camphor. (Committee on Drugs, 1992-1993. Camphor revisited: focus on toxicity. Pediatrics. 1994;94:127-128 cited in Martin D., et al. Dermal absorption of camphor, menthol, and methyl salicylate in humans. 2004 J Clin Pharm 44:1151-1157)

**Monday, February 6, 2012**

**Question:**

Inhalational anthrax is a concern with regard to the ongoing threat of terrorist use of biological agents. However anthrax is also a concern in its cutaneous and GI forms. What percent of naturally occurring cases worldwide involve cutaneous anthrax? What is the case fatality rate for cutaneous anthrax? What percent of treated cutaneous anthrax cases resolve without complications?

**Answer:**

The cited reference notes “cutaneous anthrax accounts for 95% of human cases globally. Data from pre- antibiotic and vaccine days indicated that 10—40% of untreated cutaneous anthrax cases might be expected to result in death.” With appropriate treatment, less than 1% of cases are fatal. Cutaneous anthrax can be self-limiting, and lesions resolve without complications or scarring in 80—90% of cases with treatment. (Doganay M, et al. A review of cutaneous anthrax and its outcome. 2010 J Inf Pub Health 3:98-105)

**Friday, February 3, 2012**

**Question:**

What is the most prevalent allergen known to cause allergic contact dermatitis?

**Answer:**

Nickel (Ni) is the most prevalent allergen causing allergic contact dermatitis. (Krob HA et al. Prevalence and relevance of contact dermatitis allergens: a meta-analysis of 15 years of published T.R.U.E. test data. 2004 J Am Acad Dermatol 51:349-353)

**Thursday, February 2, 2012**

**Question:**

Mercury is used in some unlabeled skin lightening creams produced in Mexico. What specific form of mercury is most often found in these skin lightening creams that are capable of resulting in skin absorption of mercury and may result in elevated levels of blood and urine mercury?

**Answer:**

Inorganic mercury (often in the form of mercurous chloride) is used in some skin lightening creams produced outside the US. This chemical acts to inhibit melanin formation when absorbed by the skin. (Mercury exposure among household users and nonusers of skin lightening creams produced in Mexico--California and Virginia, 2010. MMWR January 20,2012; 61(2):33-36)

**Wednesday, February 1, 2012**

**Question:**

What effect has been posited with regard to the use of beta blockers for patients with breast cancer?

**Answer:**

The cited reference reports "Activation of beta adrenergic receptors may be involved in breast cancer cell metastasis and taking a beta blocker has been associated with a lower risk of breast cancer recurrence and mortality". This reference further indicates that "activation of beta adrenergic receptors has been implicated in multiple steps of metastasis formation" in breast cancer studies. However, it is pointed out that no randomized controlled trial definitively testing these end points has yet been carried out. (The Medical Letter, Jan 23,2012; 54(1382):7)

**Tuesday, January 31, 2012**

**Question:**

What is the difference in mission and role between NIOSH (National Institute of Occupational Safety and Health) and OSHA (Occupational Safety and Health Administration)?

**Answer:**

As part of the CDC, NIOSH is responsible for conducting research and making recommendations for the prevention of work-related illnesses and injuries. OSHA is the main federal agency charged with the enforcement of safety and health legislation. (www.cdc.gov/NIOSH and www.osha.gov)

**Monday, January 30, 2012**

**Question:**

What is "blackjack disease"?

**Answer:**

"Blackjack disease" is a dermatitis caused by chronic dermal exposure to chromium salts that have been used to dye the green felt used to cover various gaming and gambling tables. Blackjack disease is a somewhat esoteric occupational affliction for blackjack and other casino based card dealers and croupiers. (Fisher AA. Blackjack disease and other chromate puzzles. 1976 Cutis 18(1):21-22)

**Friday, January 27, 2012**

**Question:**

What are the two primary species of imported fire ant (IFA) in the US responsible for most medical and economic effects referable to fire ants? What is the annual attack rate regarding fire ants in endemic areas? What is the range of clinical effects related to stings from fire ants?

**Answer:**

Solenopsis richteri (black IFA) and Solenopsis invicta (red IFA) are the two primary species with medical and economic ramifications in the United States. In endemic areas, the annual attack rates of IFAs exceed 30%. Typical fire ant stings begin as itchy red "welts" and progress to form pustules. Reactions may remain local but systemic allergic reactions and anaphylaxis, including systemic reactions resulting in death, can (and do) occur. (Bhutani S and Khan DA. Allergist referrals for systemic reactions to imported fire ants: a community survey in an endemic area. Ann Allergy Asthma Immunol. 2009;102:145–148)

**Thursday, January 26, 2012**

**Question:**

Scombroid poisoning, also known as "histamine fish poisoning", is related to high histamine levels in fish meat. How does the causation scenario for scombroid differ from other forms of seafood related toxicities?

**Answer:**

The cited reference notes "Scombroid poisoning is unique among the seafood toxins since it results from product mishandling rather than contamination from other trophic levels. Inadequate cooling following harvest promotes bacterial histamine production, and can result in outbreaks of scombroid poisoning." (Hungerford JM. Scombroid poisoning: a review. 2010 Toxicon 56:231-243)

**Wednesday, January 25, 2012**

**Question:**

What are "chrome holes"?

**Answer:**

Chromic acid and alkaline chromate are agents commonly encountered in the tanning and electroplating industries. These substances have a corrosive action when they enter the skin through a minor nick or break in the integument. This results in the formation of chronic, ulcerative lesions known as "chrome holes". Typically, the lesions are found on fingers, hands or forearms. "Chrome holes" also occur on the dorsal surfaces of the feet when chrome salts have been allowed to permeate boots or shoes. The lesions are usually painless and persist for many months before spontaneously healing with permanent atrophic scar. Identical lesions can also be produced by arsenic or zinc salts but these are less frequently encountered. (Williams N. Occupational skin ulceration in chrome platers. 1997 Occup Med 47(5):309-310 and <http://www.cdc.gov/niosh/topics/skin/occderm-slides/ocderm8.html>)

**Tuesday, January 24, 2012**

**Question:**

Is clinically significant methanol toxicity possible following inhalational exposure to products containing methanol?

**Answer:**

A number of reports have demonstrated that methanol toxicity can result from intentional inhalational exposure and can range from a relatively benign clinical course to death. Some have suggested that lower levels of serum methanol are achieved through inhalation versus ingestion however the cited reference reports serum methanol levels  $\geq 50$  mg/dL in 28% (n=19) of the admitted cases of inhalation exposure to methanol they report. (Wallace EA and Green AS. Methanol toxicity secondary to inhalant abuse in adult men. 2009 Clin Tox 47: 239-242)

**Monday, January 23, 2012**

**Question:**

The CDC estimates that the excessive use of alcohol accounted for approximately 80,000 deaths and 2.3 million years of potential life lost (YPLL) from 2001 through 2005. Binge drinking reportedly accounted for more than 50% of those deaths and two thirds of the YPLL. How does CDC define "binge drinking"?

**Answer:**

Binge drinking is defined as “four or more drinks for women and five or more drinks for men on an occasion during the past 30 days.” (MMWR January 13,2012, 61(1):14-19)

**Friday, January 20, 2012****Question:**

What effect may occupational exposure to styrene have on hearing in some workers?

**Answer:**

Several studies have been conducted with styrene-exposed workers in boat or fiberglass products manufacturing. Muijser et al reported that workers exposed to low levels of styrene did not appear to have increased hearing loss at high frequencies when compared to controls. The comparison of the two extreme exposure groups (low and high exposures), however, revealed a statistically significant difference in hearing thresholds at high frequencies. (Muijser H, et al. The effects of occupational exposure to styrene on high-frequency hearing thresholds. Toxicology 1988;49:331-40 as cited in Aksentijevic A et al. Audiological findings in workers exposed to styrene alone or in concert with noise. 2006 Noise and Health 8(30))

**Thursday, January 19, 2012****Question:**

What nematocide and soil fumigant, first developed in the 1950's, has been shown to irreversibly inhibit spermatogenesis in male workers who applied this chemical or otherwise came into significant contact with it?

**Answer:**

1,2-dibromo-3-chloropropane (DBCP) was used in the past as a soil fumigant and nematocide on crops; it is no longer used except as an intermediate in chemical synthesis. Acute (short-term) exposure to DBCP in humans results in moderate depression of the central nervous system (CNS) and pulmonary congestion from inhalation, and gastrointestinal distress and pulmonary edema from oral exposure. Chronic (long-term) exposure to DBCP in humans causes male reproductive effects, such as decreased sperm counts. (Winker R and Rudiger HW. Reproductive toxicology in occupational settings: an update. 2006 Int Arch Occup Environ Health 79:1-10 and <http://www.epa.gov/ttn/atw/hlthef/dibromo-.html>)

**Wednesday, January 18, 2012****Question:**

Complications of toluene abuse (sniffing) include muscular weakness, nausea, vomiting, abdominal pain, hematemesis, altered mental status, cerebellar abnormalities, and peripheral neuropathy. What renal effects have been reported to be associated with toluene abuse?

**Answer:**

A number of cases of renal tubular acidosis have been reported in association with toluene abuse by inhalation. (Streicher HZ et al Syndrome of toluene sniffing in adults. 1981 Ann Int Med 94:758-762 as cited in Kao-Chin K, et al. Hypokalemic muscular paralysis causing acute respiratory failure due to rhabdomyolysis with renal tubular acidosis in a chronic glue sniffer. 2000 Clin Tox 38(6):679-6810)

**Tuesday, January 17, 2012****Question:**

A recent Cochrane systematic review evaluated a number of trials of the efficacy of normobaric oxygen compared with hyperbaric oxygen for the protection of neurologic sequelae in individuals with acute CO poisoning. What were the conclusions of this review?

**Answer:**

This systematic review concluded “Existing randomized trials do not establish whether the administration of HBO to patients with carbon monoxide poisoning reduces the incidence of adverse neurologic outcomes. Additional research is needed to better define the role, if any, of HBO in the treatment of patients with carbon monoxide poisoning.” (Buckley NA et al. Hyperbaric oxygen for carbon monoxide poisoning. Cochrane Database of Systematic Reviews. 2011 issue 4, Art. No.: CD002041)

**Monday, January 16, 2012****Question:**

A recent Cochrane systematic review evaluated a number of trials of the efficacy of normobaric oxygen compared with hyperbaric oxygen for the protection of neurologic sequelae in individuals with acute CO poisoning. What were the conclusions of this review?

**Answer:**

This systematic review concluded “Existing randomized trials do not establish whether the administration of HBO to patients with carbon monoxide poisoning reduces the incidence of adverse neurologic outcomes. Additional research is needed to better define the role, if any, of HBO in the treatment of patients with carbon monoxide poisoning.” (Buckley NA et al. Hyperbaric oxygen for carbon monoxide poisoning. Cochrane Database of Systematic Reviews. 2011 issue 4, Art. No.: CD002041)

**Friday, January 13, 2012****Question:**

What markers are used to monitor for cardio-toxicity related to the use of anthracycline chemotherapeutic drugs such as doxorubicin?

**Answer:**

Measures of left ventricular ejection fraction (LVEF) are currently the most commonly used modalities. However, the cited reference points out that “Waiting for the LVEF to be substantially reduced to detect cardiotoxicity is not ideal, because this implies that damage has already occurred; detecting significant cardiotoxicity before it is profound enough to cause a drop in LVEF is far preferable.” The authors go on to point out that “Serum biomarker screening (particularly using cardiac troponins) is an attractive method for detecting early injury, and impressive early evidence exists for its use. However, further study is needed before routine biomarker screening is used in clinical practice. (Witteles RM et al. Chemotherapy-associated cardiotoxicity: How often does it really occur and how can it be prevented? 2011 Heart Failure Clinics 7(3):333-344)

**Thursday, January 12, 2012****Question:**

The ingestion of multiple small magnets (or toys containing magnets) can lead to a number of important gastrointestinal complications. What are they?

**Answer:**

Following ingestion of multiple small magnets the cited reference notes "When aligned, the force between magnets pulls bowel walls together, exerting pressure and causing obstruction, necrosis, fistula, and peritonitis from perforation". (Brown DJ. Small bowel perforation caused by multiple magnet ingestion. 2010 J Emerg Med 39(4):497-498)

**Wednesday, January 11, 2012****Question:**

What are the rates of survival for solid organ transplantation with organs harvested from donors who succumbed to carbon monoxide poisoning?

**Answer:**

The below cited systematic review reports heart and lung transplants procured from CO poisoned donors with or without burn had organ survival rates of 68% and 67%, respectively, while renal, pancreas and liver transplants had a 100% organ survival rate. (Busche MN, et al. Solid organ procurement from donors with carbon monoxide poisoning and/or burn - a systematic review. 2011 Burns 37:814-822)

**Tuesday, January 10, 2012****Question:**

What is the toxic component of the venom of the Black Widow spider (*Latrodectus mactans*)? What is the mechanism of action of this toxin?

**Answer:**

The toxic component of Black Widow spider venom is alpha latrotoxin. Alpha latrotoxin binds to pre-synaptic receptors (neurexin I-alpha and latrophilin). This binding triggers neurotransmitter release from presynaptic sites and results in excessive motor end plate stimulation causing muscular spasm, local sweating, piloerection, and elevated blood pressure. (Baba A and Cooper JR. The action of black widow spider venom on cholinergic mechanisms in synaptosomes. 1980 J Neurochem 34(6):1369-1379 as quoted in Murphy C, et al Anaphylaxis with *Latrodectus* antivenin resulting in cardiac arrest. 2011 J Med Tox 7(4):317-321)

**Monday, January 9, 2012****Question:**

What is the SEER program?

**Answer:**

SEER is the "Surveillance, Epidemiology, and End Results" Program of the National Cancer Institute. SEER is a premier source for cancer statistics in the United States. SEER collects information on incidence, prevalence and survival from specific geographic areas representing 28 percent of the US population. SEER also compiles reports on all of these plus cancer mortality for the entire country. (<http://seer.cancer.gov>)

**Friday, January 6, 2012****Question:**

What is the difference in the chest x-ray findings usually seen in cadmium related pneumonitis versus metal fume fever?

**Answer:**

The chest x-ray in metal fume fever is typically normal while the chest x-ray in cases of cadmium pneumonitis is frequently abnormal, often with bilateral interstitial infiltrates. (Barnhart S and Rosenstock L. Cadmium chemical pneumonitis. 1964 Chest 86(5): 789-791)

**Thursday, January 5, 2012****Question:**

Coral snakes produce less venom than pit vipers (on a weight basis), but the venom is more potent than that of all of US snakes except the Mojave rattlesnake (*Crotalus scutulatus*). Coral snake venom produces much less local tissue damage and hematological abnormalities than that of the pit vipers. What is the mechanism of action of coral snake venom?

**Answer:**

The cited reference notes that "peptides in the venom block post synaptic acetylcholine receptors and may produce severe delayed systemic effects, including paralysis, respiratory depression, and death". Morgan D., et al. Texas coral snake bites 2007 Southern Med J 100(2): 152-156)

**Wednesday, January 4, 2012****Question:**

Bleomycin is an antibiotic drug that is used in some cases as a chemotherapeutic agent in the treatment of many head and neck cancers as well as penile, testicular, cervical, and vulva cancers. What is the most feared toxicity associated with the use of this drug? What are the risk factors for bleomycin pulmonary toxicity?

**Answer:**

The most concerning toxicity associated with the drug bleomycin is pulmonary toxicity. The main symptoms of bleomycin lung toxicity include dyspnea, productive cough, thoracic pain, and pleuritic pain. The risk factors include age older than 70, high doses, pulmonary irradiation, renal insufficiency, history of smoking, G-CSF use, concomitant multiple chemotherapeutics (especially cisplatin) and the need for volume replacement intra and post operatively. Bleomycin toxicity has been reported in up to 46% of patients receiving this agent. (Azambuja E., et al. Bleomycin lung toxicity: who are the patients with increased risk? 2005 Pulm Pharm Therapeutics 18:363-366)

**Tuesday, January 3, 2012****Question:**

What percentage of elevated blood lead levels reported among adults in the US are work-related?

**Answer:**

Approximately 95% of all elevated BLLs reported among adults in the United States are work-related. (CDC. Adult blood lead epidemiology and surveillance—United States, 2008–2009. MMWR 2006;60(25): 841-845)

**Monday, January 2, 2012**

**Question:**

What are aflatoxins? How may humans be exposed to aflatoxins? Chronic exposure to aflatoxins increases the risk for what human disease?

**Answer:**

The aflatoxins are highly substituted coumarins containing a fused dihydrofurofuran moiety. There are four naturally occurring aflatoxins denoted as: B1, B2, G1, and G2. Humans may be exposed to aflatoxins by consumption of grains and foodstuffs contaminated with strains of *Aspergillus flavus* or *A. paraciticus* during growth, harvest, or storage. Chronic aflatoxin exposure substantially increases the risk for hepatocellular carcinoma in individuals who suffer from chronic hepatitis B infection. (Kensler TW, et al. Aflatoxin: A 50-year odyssey of mechanistic and translational toxicology. 2011 Tox Sci 120(S1):S28-S48)

**Friday, December 30, 2011**

**Question:**

What is the so-called “healthy worker effect”?

**Answer:**

The cited reference eloquently points out that “The healthy worker effect (HWE) is a term applied to the deficit of both morbidity and mortality ascribed to various employment-associated factors when workers and the general population are compared. The HWE reflects that an individual must be relatively healthy in order to be employable in a workforce, and both morbidity and mortality rates within the workforce are usually lower than in the general population. As a result, real excesses in both morbidity and mortality due to harmful exposures at work might be wholly or partially masked”. (Li C and F-C Sung. A review of the healthy worker effect in occupational epidemiology. 1999 Occup. Mod. 49 (4): 225-229)

**Thursday, December 29, 2011**

**Question:**

PCBs (polychlorinated biphenyls) are widespread in the environment, have been identified in the food chain, and have been verified as bio-accumulating in human breast milk. Further, breastfed infants ingest significantly higher levels of PCBs than do formula-fed infants. Does a threshold exist among the general population with regard to the presence of PCBs in breast milk beyond which the risks of breastfeeding outweigh the benefits of breastfeeding?

**Answer:**

The vast majority of results from the body of research reviewed by the author of the cited reference indicate that despite higher PCB loads, breastfed children “fare better than their formula-fed peers” and that “At this point, there is no evidence of a threshold among the general population beyond which the risks of breastfeeding outweigh the benefits, nor is there any evidence demonstrating a clinically significant negative effect of postnatal exposure to PCBs via breast milk”. (Jorissen J. Outcomes associated with postnatal exposure to PCB’s via breast milk. 2007 Adv in Neonatal Care 7(5):230-237)

**Wednesday, December 28, 2011**

**Question:**

What is radon?

**Answer:**

The cited reference answers this question as follows: “Radon is a naturally occurring, radioactive noble gas with the atomic number 86. It is odorless, tasteless, colorless, and chemically nearly inert. It is found in the radioactive decay series of uranium and thorium, in which it is formed from its mother nuclide, radium. The very long-lived parent nuclei and their breakdown products are natural components of rock and soil. A number of isotopes of radon are known, of which radon-222 is the most stable: it decays to polonium-218 with a half-life of 3.8 days”. (Schmid K, et al. Radon in indoor spaces- An underestimated risk factor for lung cancer in environmental medicine. 2010 Disch Aztebl Int 107(11):181-186)

**Tuesday, December 27, 2011**

**Question:**

Dabigatran etexilate (Pradaxa) is a relatively new anticoagulant drug that acts via direct thrombin inhibition. What is currently the only available option for reversal of the anticoagulant effects of this drug?

**Answer:**

Emergency dialysis is currently the only option to reverse the anticoagulant effects of dabigatran. (Cotton BA, et al. Acutely injured patients on dabigatran. 2011 NEJM 365:2039-2040)

**Monday, December 26, 2011**

**Question:**

IARC has classified arsenic in drinking water as a group I lung carcinogen. In addition to lung cancer, there is emerging evidence that ingested arsenic may also cause nonmalignant respiratory disease. What specific non-malignant diseases have been posited to be caused by ingested arsenic?

**Answer:**

The results of the cited study provide evidence that consuming large amounts of water containing high levels of arsenic may lead to increased risks for bronchiectasis. In addition, there may be an increase in COPD and bronchitis. The authors of this study point out that “future research is needed to confirm these findings and investigate the mechanisms by which arsenic could cause these effects”. (Mazumder D, et al. Bronchiectasis in persons with skin lesions resulting from arsenic in drinking water. 2005 Epidemiology 16(6): 760–765)

**Friday, December 23, 2011**

**Question:**

What is the usual presentation for acute boric acid poisoning?

**Answer:**

Acute boric acid poisoning usually presents with nausea, persistent vomiting, diarrhea and colicky abdominal pain. In addition, neurological symptoms may be present and include headache, tremor, irritability, delirium, seizures and, in severe cases, coma and death. The skin manifestations can include flushing and erythema of the palms, soles and gluteal region. (Corradi F, et al. A case report of massive acute boric acid poisoning. 2010 Eur J Emerg Med 17(1): 48-51)

**Thursday, December 22, 2011****Question:**

Most cadmium in the human body is bound to a small, cysteine-rich metal binding protein. What is that protein and what role does it play with regard to the potential for cadmium toxicity?

**Answer:**

The protein is metallothionein (MT) and the cited reference points out that "MT functions in Cd detoxication primarily through the high affinity binding of the metal to MT, thus [fostering] sequestration of Cd away from critical macromolecules." (Klaassen CD, et al. Metallothionein protection of cadmium toxicity. 2009 Tox Appl Pharm 238:215-220)

**Wednesday, December 21, 2011****Question:**

Wilson's Disease, also known as progressive hepatolenticular degeneration, is a genetic disorder of copper metabolism. The treatment of this disorder often requires the use of copper chelating agents. What chelating agents may be used in the treatment of Wilson's disease?

**Answer:**

The chelator of choice for Wilson's Disease has been penicillamine however some patients may receive the chelator drug trientine (Syprine) while others may receive the chemical ammonium tetrathiomolybdate as a chelator. (Ala A., et al. Wilson's Disease. 2007 The Lancet 369:397-408)

**Tuesday, December 20, 2011****Question:**

Occupational inhalational exposure to enzymes may occur in a variety of industrial settings including the baking and food preparation industries and in manufacturing of laboratory enzymatic agents. What medical issues have been associated with occupational inhalational exposure to enzymes?

**Answer:**

Airborne enzymes occurring in the general environment and in purified form in industrial production have a high allergenic potential to the airways, causing rhinitis, conjunctivitis and asthma in some cases. (Baur X. Enzymes as occupational and environmental respiratory sensitizers. 2005 Int Arch Occup Environ Health 78:279-286)

**Monday, December 19, 2011****Question:**

An accurate determination of time of death is often an important issue in forensic toxicology. What is rigor mortis and how might the presence of rigor mortis assist in the determination of the precise time of death?

**Answer:**

Rigor mortis (RM) is simply the postmortem stiffening of muscles thought to be related to build up of lactate and phosphate in muscle tissue leading to an acidic microenvironment that promotes the binding of actin and myosin to yield stiff muscles. RM occurs uniformly throughout the body but is first visible in the face and neck at 1 to 4 hours after death and in the rest of the body by 12 hours post death. RM begins to disappear at about 24 hours post death. In most cases however, the presence or absence of RM cannot be used to precisely determine the time of death. (Reddy K and Lowenstein EJ. Forensics in dermatology: Part I. 2011 J Am Acad Derm; 64:801-808)

**Friday, December 16, 2011****Question:**

What chemical may be used in the treatment of both thallium toxicity and toxicity due to cesium-137?

**Answer:**

Prussian blue may be used in the treatment of both thallium toxicity and toxicity due to cesium-137. (Thompson DF and Callen ED. Soluble or insoluble Prussian blue for radiocesium and thallium poisoning? 2004 Anns Pharmacotherapy 38:1509-1514)

**Thursday, December 15, 2011****Question:**

What are the microscopic findings that may be seen in the hair shafts of individuals who have been poisoned with thallium?

**Answer:**

One report documented that the proximal portion of hair shafts were "distorted and tapered" with a "widened zone that was remarkably dark" compared to the more distal aspects of the same hair shaft. In addition, the hair cuticle was noted to be disorganized and somewhat amorphous. Numerous "gaseous inclusions" in the proximal hair shaft were also reported. (Pelclova D., et al. Two year follow up of two patients after severe thallium intoxication. 2009 Hum Exp Toxicol 28(5):263-272)

**Wednesday, December 14, 2011****Question:**

What is TENORM and what groups of workers may be exposed to TENORM?

**Answer:**

TENORM is "technologically enhanced naturally occurring radioactive materials". Some workers in a variety of industries may be exposed to TENORM. These industries include: mining, phosphate processing, metal ore processing, heavy mineral sand processing, titanium pigment production, fossil fuel extraction, building materials manufacturing, scrap metal processing, and aviation industries. (Vearrier D, et al. Technologically enhanced naturally occurring radioactive materials. 2009 Clin Tox 47(5):393-406)

**Tuesday, December 13, 2011****Question:**

What is the odor threshold for the chemical formaldehyde?

**Answer:**

The odor threshold for formaldehyde is reported to range from 0.05 ppm to 1 ppm. (Leonardos G, et al. Odor threshold determinations of 53 odorant chemicals. 1969 J Air Pollut Control Assoc 19:91–95 and Arts J, et al. Local effects in the respiratory tract: Relevance of subjectively measured irritation for setting occupational exposure limits. 2006 Int Arch Occup Environ Health 79(4):283–298, as reported in the Addendum to the Toxicological Profile for Formaldehyde, October 2010, Agency for Toxic Substances and Disease Registry, page 4)

**Monday, December 12, 2011****Question:**

Ingestion of the substance cresol, a phenol derivative sometimes used as a disinfectant, may result in gastrointestinal corrosive injury, central nervous system and cardiovascular disturbances, respiratory distress, hepatotoxicity, and nephrotoxicity. What is the characteristic urine color change associated with cresol intoxication and what other conditions may be associated with the same urine color?

**Answer:**

The urine in cases of cresol poisoning has been reported to be black. Other conditions that may be associated with black urine include hemoglobinuria, myoglobinuria, alcaptonuria, melanuria, porphyrinuria, tyrosinuria, and malignant melanoma. Extrinsic causes include dyes in food. (Seak C, et al. A case of black urine and dark skin-cresol poisoning. 2010 Clin Tox 48:959-960)

**Friday, December 9, 2011****Question:**

The inhalation of fumes generated by mixing certain household cleaning chemicals can lead to pulmonary irritation, pulmonary injury, pneumonitis and, depending on circumstances, even death. What potentially harmful compound is generated by mixing household ammonia and bleach?

**Answer:**

Mixing bleach and ammonia releases chloramine gas; a combination of monochloramines (NH<sub>2</sub>Cl) and dichloramines (NHCl<sub>2</sub>). Inhaled chloramines can react with respiratory tract moisture releasing ammonia (NH<sub>3</sub>), hydrochloric acid (HCl), and oxygen free radicals. Inhalation of low concentrations of chloramines may cause mild respiratory tract irritation. The cited reference points out that in high concentrations, "the combination of hydrochloric acid, ammonia, and oxygen free radicals may result in corrosive effects and cellular injury, resulting in pneumonitis and edema". (Tanen DA, et al. Severe lung injury after exposure to chloramine gas from household cleaners. 1999 NEJM 341:848-849)

**Thursday, December 8, 2011****Question:**

What do the following drugs, long since withdrawn from markets around the world, have in common: Contergan, Distaval, Isomin, Softenon, Noctosediv, Glutanon, and Valgis?

**Answer:**

These drugs are all different brands of thalidomide from various countries around the world. They all were responsible for causing serious limb reduction defects in children of mothers who took the drugs during pregnancy. (Avorn J. Learning about the safety of drugs- A half century of evolution. 2011 NEJM 365:2151-2153)

**Wednesday, December 7, 2011****Question:**

What is "acid rain"?

**Answer:**

"Acid rain" is a broad term referring to a mixture of wet and dry deposition (deposited material) from the atmosphere containing higher than normal amounts of nitric and sulfuric acids. The precursors, or chemical forerunners, of acid rain formation result from both natural sources, such as volcanoes and decaying vegetation, and man-made sources, primarily emissions of [sulfur dioxide \(SO<sub>2</sub>\)](#) and [nitrogen oxides \(NO<sub>x</sub>\)](#) resulting from fossil fuel combustion. In the United States, roughly 2/3 of all SO<sub>2</sub> and 1/4 of all NO<sub>x</sub> come from electric power generation that relies on burning fossil fuels, like coal. Acid rain occurs when these gases react in the atmosphere with water, oxygen, and other chemicals to form various acidic compounds. The result is a mild solution of sulfuric acid and nitric acid. (www.epa.gov)

**Tuesday, December 6, 2011****Question:**

Cocaine is known to activate circulating platelets. What is the proposed mechanism for this effect?

**Answer:**

Cocaine activates circulating platelets by increasing expression of platelet factor 4, thromboglobulin B and P-selectin. (Finkel J and Marhefka G. Rethinking cocaine-associated chest pain and acute coronary syndrome. 2011 Mayo Clin Proc 86(12):1198-1207)

**Monday, December 5, 2011****Question:**

What is SAMHSA and what are the four centers contained in its organizational structure?

**Answer:**

SAMHSA, the Substance Abuse and Mental Health Administration, was established in 1992 and directed by Congress to effectively target substance abuse and mental health services to the people most in need and to translate research in these areas more effectively and more rapidly into the general health care system. The four centers are: 1- The Center for Mental Health Services (CMHS), 2- The Center for Substance Abuse Prevention (CSAP), 3- The Center for Substance Abuse Treatment (CSAT) and 4- the Center for Behavioral Health Statistics and Quality (CBHSQ) (www.samhsa.gov)

**Friday, December 2, 2011****Question:**

Sudden releases of large clouds of carbon dioxide (CO<sub>2</sub>) gas from two lakes claimed the lives of more than 1800 people by asphyxiation. What were the names of the lakes involved and in what country are these lakes located?

**Answer:**

These gas-charged lakes were Lake Nyos and Lake Monoun in Cameroon. The Lake Nyos event occurred in 1986 and the Lake Monoun event occurred in 1984. (Kling GW et al. Degassing Lakes Nyos and Monoun: Defusing certain disaster. 2005 PNAS 102(40):14185-14190)

**Thursday, December 1, 2011**

**Question:**

Sphingomyelinase D is the main toxic component responsible for venom toxicity in what species of spider?

**Answer:**

Sphingomyelinase D is the main toxic component responsible for venom toxicity in *Loxoscles* species. The authors point out that this enzyme “leads to local lesions by thrombus formation and migration of white blood cells and is responsible for intravascular hemolysis through alterations in the red cell membrane...”. (de Roodt A, et al. Toxicity of two North American *Loxoscles* venoms and their neutralization by antivenoms. 2007 Clin Tox 45(6):678-687)

**Wednesday, November 30, 2011**

**Question:**

What is "phossy jaw" and in what U.S. occupational cohort was this disorder first recognized?

**Answer:**

Phossy jaw refers to the condition of mandibular osteonecrosis that may develop in individuals who may be occupationally exposed to white phosphorus (sometimes referred to as yellow phosphorus). Phossy jaw was first identified in workers in the white phosphorus match production industry. (Vance MA. Osteonecrosis of the jaw and bisphosphonates: A comparison with white phosphorus, radium, and osteopetrosis. 2007 Clin Tox 45(7):753-762)

**Tuesday, November 29, 2011**

**Question:**

Both zinc and aluminum phosphides are extremely effective rodenticides and insecticides. Where are these chemicals generally used and what is the active chemical that functions as the primary pesticide when these chemicals are used?

**Answer:**

Aluminum and zinc phosphides are usually used to protect grain stored in the holds of ships and in large containers wherein grain is transported. These phosphides are mixed with the grains and they interact with moisture in the atmosphere in the air in and around the grains to liberate phosphine (hydrogen phosphide, phosphorus trihydride). Phosphine acts as the active pesticide. (Proudfoot AT. Aluminum and zinc phosphide poisoning. 2009 47(3):89-100)

**Monday, November 28, 2011**

**Question:**

What are the three main toxic syndromes associated with organophosphate poisoning?

**Answer:**

The three main toxic syndromes associated with organophosphate poisoning are 1- acute cholinergic syndrome, 2- intermediate syndrome, and 3- organophosphate induced delayed polyneuropathy (OPIDN). (Jayawardane P, et al. Electrophysiological correlates of intermediate syndrome following acute organophosphate poisoning. 2009 Clin Tox 47(3):193-205)

**Friday, November 25, 2011**

**Question:**

When does the decrease in platelet count associated with heparin- induced thrombocytopenia (HIT) typically begin?

**Answer:**

The decrease in platelet count typically associated with HIT begins 5-14 days after starting heparin. (Selleng K, et al. Heparin-induced thrombocytopenia in intensive care patients. 2007 Crit Care Med 35(4):1165-1176)

**Thursday, November 24, 2011**

**Question:**

What chemical threat agent has been known as Yperite, Hunstoffs, distilled, Yellow Cross and “L-O-S-T”?

**Answer:**

The chemical is bis[2-chloroethyl] sulfide or sulfur mustard (SM). The cited reference indicates “the French named it Yperite. SM was also referred to as “lost,” an acronym from the first letters of the chemists Lommel and Steinkopf, who investigated the military use of the compound; “Yellow Cross,” because of the markings on German munitions containing SM, and HD (from Hunstoffs, distilled), the designated acronym used by the U.S. military”. (Shakarjian MP et al. Mechanisms mediating the vesicant actions of sulfur mustard after cutaneous exposure. 2010 Tox Sci 114(1):5-19)

**Wednesday, November 23, 2011**

**Question:**

The clinical use of barbiturates is decreasing yet severe cases of barbiturate poisoning do still occur. What is the main goal of enhanced elimination techniques when applied to the treatment of barbiturate poisoning?

**Answer:**

The cited reference indicates that mortality from barbiturate poisoning is generally low with the use of supportive care alone. The authors point out that the main aim of enhanced elimination is “to reduce the duration of admission and to minimize complications of prolonged intubation and intensive care admission.” The authors note, however, that these potential benefits have not yet been confirmed. (Roberts D and Buckley N. Enhanced elimination in acute barbiturate poisoning-A systematic review. 2011 Clin Tox 49(1):2-12)

**Tuesday, November 22, 2011**

**Question:**

What are the typical presentations associated with the disorder known as the Syndrome of Irreversible Lithium-Effectuated Neurotoxicity (SILENT)?

**Answer:**

The typical presentations for SILENT include 1- persisting cerebellar dysfunction; 2- Persisting extrapyramidal syndromes; 3- persisting brainstem dysfunction; and 4- dementia with varying degrees of organic mental syndromes. Atypical presentations for SILENT (such as nystagmus, retrolubar optic neuritis, persisting papilledema, choreoathetoid movements, peripheral neuropathies, myopathy and central pontine myelinolysis) have also been reported. (Adityanjee et al. The syndrome of irreversible lithium-effectuated neurotoxicity. 2005 Clin Neuropharmacol 28(1):38-49)

**Monday, November 21, 2011**

**Question:**

According to the Centers for Disease Control and Prevention, individuals consuming non-commercially harvested shellfish taken from Alaskan waters recently are at risk for what toxin induced disorder?

**Answer:**

CDC has recently warned against the consumption of non-commercially harvested shellfish taken from Alaskan waters due to the risk of paralytic shellfish poisoning (PSP). PSP primarily results from ingestion of saxitoxins, toxins produced by marine dinoflagellate algae that accumulate in bivalve mollusks (e.g., butter clams, cockles, geoducks, and mussels). PSP is a potentially fatal neuroparalytic condition. Signs and symptoms of PSP range from mild, short-lived paresthesias of the mouth or extremities to severe, life-threatening paralysis. (MMWR, November 18, 2011/ 60(45):1554-1556).



**Friday, November 18, 2011**

**Question:**

Methylene blue is well known by clinical toxicologists as an antidote for methemoglobinemia however there are numerous other clinical uses described in the medical literature for this agent. What are the other clinical uses discussed for methylene blue?

**Answer:**

Some clinical uses of methylene blue recently reported in the literature include the treatment of vasodilatory hypotension associated with anaphylaxis, sepsis, liver transplantation, hepatopulmonary syndrome, or cardiopulmonary bypass and encephalopathy induced by either ifosfamide or ackee fruit. In addition trials have been reported using methylene blue for the treatment of cognitive dysfunction in bipolar disorder. (Ng B and Cameron A. The role of methylene blue in serotonin syndrome: A systematic review) 2010 Psychosomatics 51(3):194-200)

**Thursday, November 17, 2011**

**Question:**

What is “gas eye”?

**Answer:**

“Gas eye” is a form of keratoconjunctivitis that may be seen in some workers who may be exposed to low levels of hydrogen sulfide (e.g. in some sour gas plants). The cited reference discusses an interesting aspect of this problem in that it “can be associated with reversible chromatic distortion and visual changes. This effect is sometimes accompanied by blepharospasm, tearing and photophobia”. (Guidotti TL. Hydrogen sulphide. 1996 Occ Med 46(5):367-371)

**Wednesday, November 16, 2011**

**Question:**

Warnings regarding the carcinogenic potential of the drug pioglitazone (Actos) have been issued by the European Medicines Agency as well as the US FDA. What form of cancer has been warned about with regard to this drug?

**Answer:**

The warnings noted above have involved the potential for an association between pioglitazone and bladder cancer. (Hillaire-Buys D, et al. Pioglitazone and bladder cancer. 2011 The Lancet 378(9802):1543)

**Tuesday, November 15, 2011**

**Question:**

What is the McConnell missile incident and what chemical toxicant was at issue in this incident?

**Answer:**

One of the earliest disasters attributed to nitrogen dioxide was the McConnell missile incident, which took place in the late 1970’s. Three personnel were exposed to high concentrations of nitrogen dioxide after a spill during rocket fueling. One died immediately and 2 developed a severe respiratory distress syndrome. Six others in the vicinity reportedly had dyspnea, cough, and hemoptysis, whereas the remaining 13 people remained asymptomatic. (Chen T, et al. Outdoor air pollution: Nitrogen dioxide, sulfur dioxide, and carbon monoxide health effects. 2007 Am J Med Sci 333(4):249-256)

**Monday, November 14, 2011**

**Question:**

The characteristic response of human skin contacted by sulfur mustard (SM) involves the delayed onset of erythema followed by infiltration of the affected area with inflammatory cells and the development of local edema. This is followed by the development of blisters of variable size and a subsequent prolonged period for resolution and healing. What is the generally understood mechanism for the development of the skin blisters commonly associated with sulfur mustard cutaneous exposure?

**Answer:**

The cited reference points out that SM is a bifunctional alkylating agent which reacts with many targets including lipids, proteins, and DNA, forming both intra- and intermolecular cross-links. Despite the relatively nonselective chemical reactivity of this agent, basal keratinocytes are more sensitive, and blistering involves detachment of these cells from their basement membrane adherence zones. (Shakarjian MP, et al. Mechanisms mediating the vesicant actions of sulfur mustard after cutaneous exposure. 2010 Tox Sci 114(1):5-19)

**Friday, November 11, 2011**

**Question:**

Drinking water supplies in the US were traditionally disinfected using free chlorine. However free chlorine can react with organic compounds in water to form trihalomethanes which EPA regulations limit to 80 micrograms per liter. As a result many municipal water companies were forced to consider alternatives to free chlorine. What is the most commonly used alternative and why is it used?

**Answer:**

The most commonly used alternative to free chlorine is monochloramine and it is used because it does not react as readily (as does free chlorine) with organic compounds to form trihalomethanes. (Ward RA. Avoiding toxicity from water borne contaminants in hemodialysis: New challenges in an era of increased demand for water. 2011 Ad in Chronic Kid Dis, 18(3):207-213)

**Thursday, November 10, 2011**

**Question:**

Is there an increased risk for the development of serious cardiovascular events (sudden death, stroke, myocardial infarction) associated with the use of ADHD drugs in children and young adults?

**Answer:**

A recently published study of more than 1,200,000 children and young adults between ages 2 and 24 years (mean age 11.1 years of age) showed “no evidence that current use of an ADHD drug was associated with an increased risk of serious cardiovascular events, although the upper limit of the 95% confidence interval indicated that a doubling of the risk could not be ruled out. However, the absolute magnitude of such an increased risk would be low.” (Cooper WO, et al. ADHD drugs and serious cardiovascular events in children and young adults. This article (10.1056/NEJMoa1110212) was published on November 1, 2011, at www.NEJM.org)

**Wednesday, November 9, 2011**

**Question:**

What is byssinosis?

**Answer:**

Byssinosis is a respiratory disorder of cotton mill workers and is characterized by chest tightness, cough, shortness of breath and difficulty breathing 1-2 hours after the affected individual returns to work after several days off. Symptoms often resolve overnight and become milder on subsequent days. It is hypothesized that this occupational illness is causally related to respirable cotton dust contaminated with endotoxins. (Altin R. et al. Prevalence of byssinosis and respiratory symptoms among cotton mill workers. 2002 Respiration 69:52-56)

**Tuesday, November 8, 2011**

**Question:**

What is the difference between inhibition of platelet aggregation induced by orally ingested aspirin as compared with topically applied methyl salicylate?

**Answer:**

The cited reference reports that topically applied methyl salicylate and orally ingested aspirin both significantly decreased platelet aggregation in healthy human volunteers. In addition, no significant difference was detected between baseline and 6-hour thromboxane levels for either aspirin or methyl salicylate. (Tanen DA, et al Comparison of oral aspirin versus topical applied methyl salicylate for platelet inhibition. 2008 Ann Pharmacother, 42:1396-1401)

**Monday, November 7, 2011**

**Question:**

Ziprasidone (Geodon, Zeldox), is an atypical antipsychotic agent for the treatment of schizophrenia. This drug undergoes extensive metabolism in humans with only about 5% of the dose excreted as unchanged drug. How is this drug metabolized?

**Answer:**

Two enzyme systems have been implicated in ziprasidone metabolism. The cited reference points out that aldehyde oxidase, a cytosolic enzyme, catalyzes the primary reductive pathway, and cytochrome P4503A4 (CYP3A4) is responsible for two alternative oxidation pathways. The involvement of two competing pathways in ziprasidone metabolism greatly reduces the potential for pharmacokinetic interactions between ziprasidone and other drugs. (Beedham C, et al. Ziprasidone metabolism, aldehyde oxidase and clinical implications. 2003 J Clin Psychopharm, 23:229-232)

**Friday, November 4, 2011**

**Question:**

Warfarin induced dermal necrosis is a rare phenomenon occurring in less than 0.1 percent of patients taking the drug. Which patients are most likely to develop this relatively rare condition and what is the most common anatomic distribution for skin lesions related to this disorder?

**Answer:**

Warfarin induced skin necrosis is seen primarily in middle aged, perimenopausal, obese females being treated for deep vein thrombosis or pulmonary embolism. The early symptoms afflicting the skin usually appear within the first ten days following starting warfarin and most lesions develop between day 3 and day 6 of therapy. The distribution of lesions in this disorder is random but the breast is the most common site followed by the buttocks and the thighs. (Chan YC et al. Warfarin induced skin necrosis. 2000 Br J Surg 87:266-272)

**Thursday, November 3, 2011**

**Question:**

What are the locations within the United States where the US Army stores or has stored chemical weapons?

**Answer:**

The nine locations within the United States where the US Army stores or has stored chemical weapons include: Umatilla, OR (Umatilla Chemical Depot); Tooele, UT (Deseret Chemical Depot); Pueblo, CO (U.S. Army Pueblo Chemical Depot); Anniston, AL (Anniston Army Depot); Richmond, KY (Blue Grass Army Depot); Newport, IN (Newport Chemical Depot); Pine Bluff, AR (Pine Bluff Arsenal); Edgewood, MD (Edgewood Area of Aberdeen Proving Ground); and Johnston Island (Johnston Atoll Chemical Agent Disposal System) (U.S. Army Chemical Materials Agency: <http://www.cma.army.mil/home.aspx>)

**Wednesday, November 2, 2011**

**Question:**

Why is heroin not usually sought for detection in the ordinary clinical lab setting? What heroin metabolite is usually considered to be proof of recent heroin use and what is the usual period of detectability for this heroin metabolite?

**Answer:**

The cited reference notes the half-life of heroin in plasma is reported to be brief, only about 2 to 8 minutes, because it is rapidly metabolized by cholinesterase and arylesterase to 6-monoacetylmorphine (6-MAM). As a result, heroin per se is not usually sought in the ordinary clinical lab setting. The half-life of the metabolite, 6-MAM, has been reported to be 10 to 40 minutes, and it may be detectable from 2 hours to up to 24 hours after heroin use. (von Euler, et al. Interpretation of the presence of 6-monoacetylmorphine in the absence of morphine-3-glucuronide in urine samples: Evidence of heroin abuse. 2003 Ther Drug Monitoring 25:645-648)

**Tuesday, November 1, 2011**

**Question:**

During the most recent CDC reporting year for surveillance of waterborne illness (2007-2008) only one (1) outbreak was attributable to chemical contamination of drinking water. What was the chemical at issue and what were the circumstances of this outbreak?

**Answer:**

The single outbreak attributable to chemical contamination of drinking water involved 145 cases of illness following exposure to water containing high concentrations of sodium hydroxide. This outbreak occurred within a public water system after a sodium hydroxide overflow at the water treatment facility raised the pH of the drinking water. No deaths were attributed to this incident. (MMWR September 23, 2011, 60(12):1-75)

**Friday, October 28, 2011**

**Question:**

The lifetime risk of prostate cancer in the USA is estimated to be approximately 16%. What is the effect of dietary supplementation with vitamin E with regard to prostate cancer among healthy men?

**Answer:**

A recent long-term follow up study including more than 35,000 men in the US, Canada and Puerto Rico reported that dietary supplementation with vitamin E significantly increased the risk for prostate cancer among healthy men. (Klein EA. et al. Vitamin E and the risk of prostate cancer- the selenium and vitamin E cancer prevention trial (SELECT). 2011 JAMA 306(14):1549-1556)

**Thursday, October 27, 2011**

**Question:**

What is the current experience regarding the potential for teratogenicity in patients who have been treated with arsenic trioxide?

**Answer:**

The cited reference notes that Mathews et. al. (Mathews V, et al. Single-agent arsenic trioxide in the treatment of newly diagnosed acute promyelocytic leukemia: long-term follow-up data. J Clin Oncol. 2010; 28(24):3866-3871) reported that despite counseling against pregnancy after therapy, in view of the absence of data on effect of prior arsenic trioxide therapy and teratogenicity, 7 patients (4 women and 3 men) have had 8 normal babies. (Chen S, et al. From an old remedy to a magic bullet: molecular mechanisms underlying the therapeutic effects of arsenic in fighting leukemia. 2011 Blood 117:6425-6437)

**Wednesday, October 26, 2011****Question:**

Acute illness and injury from swimming pool disinfectants and other chemicals used for swimming pool maintenance are not uncommon events in the United States. What is the locale for the majority of reported incidents of acute illness and injury from these chemicals?

**Answer:**

Cases of acute illness and injury from swimming pool disinfectants and other chemicals used for swimming pool maintenance are most frequently reported at private residences followed by non-manufacturing facilities including hotels and health clubs. (MMWR, October 7, 2011, 60(39):1343-1347)

**Tuesday, October 25, 2011****Question:**

The ongoing trial of Dr. Conrad Murray has focused attention on the inappropriate use of the drug propofol. The main problems noted in the routine and appropriate medical use of propofol are pain on injection and bacterial contamination. What specific aspect of the drug is causally related to both of these problems? What formulation of propofol has largely solved both of these problems?

**Answer:**

Pain on injection and bacterial contamination are related to the lipid emulsion formulation of the drug. The drug Lusedra (fospropofol) is a water soluble prodrug of propofol that acts similarly to propofol without pain on IV injection and without significant potential for contamination. (The Medical Letter, 53(1375):84)

**Monday, October 24, 2011****Question:**

Calcium supplementation is recommended to prevent post-menopausal osteoporosis in women with inadequate dietary calcium. Do calcium supplements increase the risk of myocardial infarction?

**Answer:**

The cited reference, discussing recent meta-analyses on the topic, reports that "the best data available indicate that taking calcium supplements to prevent osteoporosis does not increase or decrease the risk of cardiovascular disease." (The Medical Letter, 53(1375):83)

**Friday, October 21, 2011****Question:**

Approximately 60% of patients experience pain on initial injection of the drug propofol. What is the most efficacious means for preventing the pain associated with propofol injection?

**Answer:**

A recent study identified six efficacious interventions that are commonly used: lidocaine-propofol admixture; pre- treatment using lidocaine (without venous occlusion), opioids, non-steroidal anti-inflammatory drugs, or ketamine; and a propofol emulsion containing medium and long chain triglycerides. However, the most efficacious means identified was selecting an antecubital vein instead of a hand vein for the administration of the drug. (Jalota L, et al. Prevention of pain on injection of propofol: systematic review and meta-analysis. 2011 BMJ 342(d1110): 1-18)

**Thursday, October 20, 2011****Question:**

What is the Sentinel Event Notification System for Occupational Risk (SENSOR) program?

**Answer:**

The mission of the Sentinel Event Notification System for Occupational Risk (SENSOR) program is to build and maintain occupational illness and injury surveillance capacity within state health departments. Under this program, NIOSH provides cooperative agreement funding and technical support to state health departments to conduct surveillance on one or more occupational illnesses or injuries. One of the illnesses supported under SENSOR is acute occupational pesticide-related illness and injury. (<http://www.cdc.gov/niosh/topics/pesticides/overview.html>)

**Wednesday, October 19, 2011****Question:**

What is the so-called "red tide toxin"?

**Answer:**

Brevetoxin, a potent neurotoxin that activates voltage sensitive sodium channels, is a red algae toxin known as the "red tide toxin". (Richards I and Bourgeois M. Red tide toxin produces in vitro depolarization of human airway smooth muscle. 2010 Clin Tox 48:121-123)

**Tuesday, October 18, 2011****Question:**

Cigarette smoking is the most consistently established causal risk factor for renal cell cancer. What percentage of renal cell carcinomas are probably caused by smoking in males? In females?

**Answer:**

The cited reference reports it is estimated that 20% to 30% of renal cell cancers in men and 10% to 20% of renal cell cancers in women are caused by cigarette smoking. (Ray G, et al. Cigarettes smoking as a cause of cancers other than lung cancer. 2010 Chest 138:491-499)

**Monday, October 17, 2011****Question:**

The Office of the Surgeon General of the US Army, in 2005, required that soldiers deployed in a war zone carry a hemostatic bandage (HemCon). What is this product made of, what is its purpose, and what effect does this bandage have on military personnel who may use it if they have shellfish allergy?

**Answer:**

HemCon is a bandage used to provide effective hemostasis and arrest of arterial bleeding. The bandage is made from chitosan, a naturally occurring compound derived from the shells of the pink North Atlantic shrimp; *Pandalus borealis*. A recent study of individuals with shellfish allergy (IgE) who were challenged with this bandage reportedly showed no clinically important adverse or allergic reactions. (Waibel KH, et al. Safety of chitosan bandages in shellfish allergic patients. 2011 Mil Med 176(10):1153-1156)

**Friday, October 14, 2011****Question:**

What biomarkers have been used in occupationally based studies investigating the chronic effects of the chemical styrene?

**Answer:**

The cited reference notes that in the occupational studies that are the basis for quantifying the relationship between chronic styrene exposure and health effects, end-of-shift or next-morning urine levels of mandelic acid and phenylglyoxilic acid may be used. Additional styrene biomarkers include urinary styrene and mercapturic acid levels as well as phenylglycine and 4-vinylphenol conjugates. (Rueff J, et al. Genetic effects and biotoxicity monitoring of occupational styrene exposure. 2009 Clinica Chimica Acta 399:8-23)

**Thursday, October 13, 2011****Question:**

Toxicity related to what chemical led to the Federal Food, Drug and Cosmetic Act of 1938?

**Answer:**

The first reported cases of diethylene glycol intoxication in the United States in 1937 were directly responsible for the creation of the Federal Food Drug and Cosmetic Act in 1938. (Wax PM. Elixirs, diluents, and the passage of the 1938 Federal Food, Drug and Cosmetic Act. 1995 Ann Int Med, 122: 456-461 as cited in Reddy N, et al. Delayed neurological sequelae from ethylene glycol, diethylene glycol and methanol poisonings. 2010 Clin Tox 48:967-973)

**Wednesday, October 12, 2011****Question:**

Eosinophilic colitis is a rare condition characterized by eosinophilic infiltration of the colonic mucosa. Drugs are the primary cause for this uncommon condition. Which drugs are most commonly associated with this condition?

**Answer:**

The following drugs are most commonly associated with the development of eosinophilic colitis: NSAIDS, carbamazepine, clozapine, cyclosporine, salicylates, sulfasalazine, elemental gold, gemfibrozil, methylprednisolone, perazine, rifampin, tacrolimus, and trimethoprim/sulfa. (Ehrenpreis ED, et al. Colonic effects of drugs, toxins and herbals. 2011 Disease-a-Month, 57(9):453-526)

**Tuesday, October 11, 2011****Question:**

Benzo[a]pyrene is an aromatic hydrocarbon that has been identified as a carcinogen. What is the primary source for this chemical and what cancer types (by organ) have been linked to benzo[a]pyrene exposure?

**Answer:**

Benzo[a]pyrene is found in cigarette smoke, coal tar, and certain roofing materials. Benzo[a]pyrene exposure has been causally linked to cancer of the stomach, skin and lung. (Luch A. Nature and nurture-Lessons from chemical carcinogenesis. 2005 Nature Reviews, 5:113-125)

**Monday, October 10, 2011****Question:**

How is lidocaine metabolized and what is the relative toxicity of the metabolites formed?

**Answer:**

According to the cited reference, lidocaine is metabolized by the cytochrome P-450 CYP3A4 isoenzyme to monoethylglycinexylidide and to glycine xylidide. Monoethylglycinexylidide is approximately 80 to 90 percent as potent an antiarrhythmic drug as lidocaine, and its relative toxicity is approximately equal to that of lidocaine, whereas glycine xylidide is 10 percent as potent. (Kenkel JM, et al. Pharmacokinetics and Safety of Lidocaine and Monoethylglycinexylidide in Liposuction. 2004 Plast. Reconstr. Surg. 114: 516-524)

**Friday, October 7, 2011****Question:**

What characterizes cases of status asthmaticus triggered by the inhalation of heroin?

**Answer:**

Common features of cases of status asthmaticus triggered by the inhalation of heroin include a history of pre-existing asthma, the sudden and severe nature of the exacerbations, the general lack of responsiveness to beta-agonists, and peripheral blood eosinophilia. (Cygan J, et al. Inhaled heroin induced status asthmaticus: Five cases and a review of the literature. 2000 Chest 117:272-275)

**Thursday, October 6, 2011****Question:**

What chemical additive, used in the past and added to gasoline as an oxygenate, has been used clinically in the treatment of gallstones?

**Answer:**

The cited reference reports: As an alternative to surgical removal of the gall bladder (cholecystectomy), dissolution of cholesterol stones in the gall bladder and bile duct has been achieved using methyl tert-butyl ether (MTBE) administered via percutaneous transhepatic catheter or endoscope. (Phillips S, et al. Epidemiology, Toxicokinetics, and Health Effects of Methyl tert-Butyl Ether (MTBE). 2008 J Med Tox 4(2): 115-126)

**Wednesday, October 5, 2011****Question:**

The FDA has urged physicians to prescribe varenicline (Chantix) for smoking cessation with caution in what groups of patients?

**Answer:**

The FDA has urged physicians to prescribe varenicline (Chantix) for smoking cessation with caution in patients with clinically significant renal compromise, patients undergoing dialysis and patients with serious psychiatric illness. (Fiore MC, et al. Treating smokers in the health care setting. 2011 NEJM 365(13):1222-1231)

**Tuesday, October 4, 2011****Question:**

What are the recognized nephrotoxic effects of NSAIDS?

**Answer:**

The cited reference indicates the recognized nephrotoxic effects of NSAIDS exist in three forms: 1- acute tubulointerstitial nephritis; 2- acute ischemic renal injury due to inhibition of the intrarenal synthesis of vasodilatory prostaglandins, and 3- (rarely) glomerular injury with large amounts of proteinuria. (Cunningham J, et al. Case 30-2011: A 62 year old woman with renal failure. 2011 NEJM 365(13):1233-1243)

**Monday, October 3, 2011****Question:**

What are the physicochemical properties believed to be the important determinants of biological response related to nanoparticles?

**Answer:**

The physicochemical properties believed to be the important determinants of biological response related to nanoparticles are: 1) particle size, 2) particle shape, 3) oxidant generation, 4) Surface functionalization, and 5) rate of dissolution. (Castronova V. Overview of current toxicological knowledge of engineered nanoparticles. 2011 J Occ Env Med., 53(6)[Suppl]: S14-S17)

**Friday, September 30, 2011****Question:**

Hypercalcemia is a rare, but reported, complication of chronic vitamin A toxicity. What are the more common manifestations of chronic vitamin A toxicity?

**Answer:**

The most common clinical manifestations of chronic vitamin A toxicity include skeletal pain, hair loss, anorexia, pseudotumor cerebri, liver disease, and psychiatric complaints. (Lippe B et al. Chronic vitamin A intoxication. 1981 Am J Dis Child, 135:634-636) as cited in (Bhalla K, et al. Hypercalcemia caused by iatrogenic hypervitaminosis A. 2005 J Am Diet Assoc, 105:119-121)

**Thursday, September 29, 2011****Question:**

What is chloracne?

**Answer:**

The authors of the cited reference note that chloracne is a persistent eruption of comedones and epidermal cysts, typically around the eyes, malar areas of the face, behind the ears, and on the scrotum in males. Chloracne has been associated with substantial exposures to chlorinated hydrocarbon compounds such as 2,3,7,8-tetrachlorodibenzo- p-dioxin (TCDD) and others. Bradshaw T and Bell D. Relevance of the aryl hydrocarbon receptor (AhR) for clinical toxicology. 2009 Clin Tox 47:632-642)

**Wednesday, September 28, 2011**

**Question:**

What usually self-limited, occupationally-based, flu-like illness, constitutes the most common acute respiratory illness for workers involved in welding processes?

**Answer:**

Metal fume fever (sometimes called Monday morning syndrome, foundry fever, smelter shakes, or welders ague) is the most common occupationally-based acute respiratory illness in welders. (Antonini JM, et al. Pulmonary effects of welding fumes: Review of worker and experimental animal studies. 2003 Am J Ind Med, 43:350-360)

**Tuesday, September 27, 2011**

**Question:**

What are the two most important toxicologic hazards faced by individuals engaged in mining operations at high altitude?

**Answer:**

The inhalation of diesel exhaust fumes along with carbon monoxide (CO) pose the most pressing toxicologic threats to miners working at high altitude. Diesel emissions at altitude contain more CO than at sea level due to increased incomplete combustion of fuel. (Vearrier D and Greenberg M. Occupational health of miners at altitude. 2011 Clin Tox 49(7):629-640)

**Monday, September 26, 2011**

**Question:**

Acute gout is often treated with the drug colchicine. This drug has also been used in the the treatment of Behcet's disease, familial Mediterranean fever, amyloidosis, psoriasis as well as recurrent pericarditis of unknown etiology. From where is colchicine derived?

**Answer:**

Colchicine is derived from the plant Colchicum autumnale also known as the autumn crocus, meadow saffron or naked lady. (Mullins M, et al. Unrecognized fatalities related to colchicine in hospitalized patients. 2011 Clin Tox, 49(7):648-652)

**Friday, September 23, 2011**

**Question:**

Formaldehyde is used in the manufacture of a variety of products including consumer appliances, porcelain-like dishware and insulation, and as a tissue preservative or bactericide in embalming uid and medical laboratories. The International Agency for Research on Cancer (IARC) classifies formaldehyde as a human carcinogen capable of causing which cancer?

**Answer:**

The International Agency for Research on Cancer (IARC) classifies formaldehyde as a human carcinogen capable of causing nasopharyngeal cancer. (Zhang L., et. al. Formaldehyde and Leukemia: Epidemiology, Potential Mechanisms, and Implications for Risk Assessment. 2010 Env Mol Mutagenesis, 51(3):181-191)

**Thursday, September 22, 2011**

**Question:**

Mycotoxins are secondary metabolites produced by some fungi. Mycotoxins may contaminate agricultural products either before harvest or under certain post-harvest conditions. One important group of food borne mycotoxins are the fumonisins. What health effects may be associated with consumption of fumonisins?

**Answer:**

Consumption of fumonisin has been associated with an increased incidence of human esophageal cancer in some parts of Africa, Central America, and Asia as well as among the African-American population in Charleston, South Carolina, USA. In addition, fumonisin consumption has been implicated in neural tube defects in human infants as fumonisin B1 reduces uptake of folate in various cell lines. (Wagacha JM and Muthomi JW. Mycotoxin problem in Africa: Current status, implications to food safety and health and possible management strategies. 2008 Int J Food Micro, 124:1-12)

**Wednesday, September 21, 2011**

**Question:**

Which xenobiotics are generally considered to be candidates for enhanced excretion by the use of urinary alkalization?

**Answer:**

The cited reference lists the following xenobiotics as capable of enhanced excretion by the use of urinary alkalization include salicylates, chlorpropamide, 2,4-dichlorophenoxyacetic acid, diflunisal, fluoride, Mecoprop (MCP, a chlorphenoxy herbicide) methotrexate, and phenobarbital. (Levine M, et al. Toxicology in the ICU: Part I: General overview and approach to treatment. 2011 Chest 140(3):795-806)

**Tuesday, September 20, 2011**

**Question:**

Carisoprodol (Soma, Soporadol, Vanadom) is a central nervous system depressant with sedative and skeletal muscle relaxant effects. What is the pharmacology of that accounts for the sedative effects of this drug?

**Answer:**

The sedative as well as the adverse effects of carisoprodol are likely due to its metabolic conversion to meprobamate. Meprobamate induces sedation via action at gamma-aminobutyric acid A receptors (Fass JA. Carisoprodol legal status and patterns of abuse. 2010 Ann Pharmacother, 44:1962-1967)

**Monday, September 19, 2011**

**Question:**

During the early 1930s, the pharmaceutical company, Squibb, Inc., began marketing a new drug called Intocostarin. What was Intocostarin and what was it first used for in the clinical setting?

**Answer:**

Intocostarin was a mixed extract of quaternary alkaloids but its main constituent was d-tubocurarine and was used as an adjunct in electroconvulsive therapy. (Lee MR. Curare: the South American arrow poison. 2005 J R Coll Physicians Edinb. 35:83-92)

**Friday, September 16, 2011**

**Question:**

The seeds of some fruit trees contain cyanogenic glycosides that may liberate cyanide when digested. What fruit trees are included in this group?

**Answer:**

Malus (apple), Prunus (cherry, plum, peach, apricot) as well as Hydrangea contains cyanogenic glycosides. (Petersen DD. Common plant toxicology: A comparison of national and Southwest Ohio data trends on plant poisonings in the 21st century. 2011 Tox Appl Pharm 254:148-153)

**Thursday, September 15, 2011**

**Question:**

What is the best way to determine if a postmortem ethanol level reflects ante-mortem alcohol ingestion or post mortem alcohol fermentation?

**Answer:**

Per Hepler et al, as cited in the below reference, vitreous humor may be used as a testing substrate to differentiate pre-mortem alcohol ingestion from post mortem alcohol fermentation as fermentation generally does not occur to any appreciable degree in the eye. (Skopp G. Preanalytic aspects in postmortem toxicology. 2004 For Sci Int, 142:75-100) (B.R. Hepler, D.S. Isenschmid, Specimen selection, collection, preservation, and security, in: S.B. Karch (Ed.), Drug Abuse Handbook, CRC Press, Boca Raton, 1998, pp. 873 889.)

**Wednesday, September 14, 2011**

**Question:**

What is the Coburn-Forster-Kane model?

**Answer:**

The Coburn-Forster-Kane (CFK) model is a tool that can be used to predict steady-state blood carboxyhemoglobin levels that correspond to a given continuous inhalation exposure to carbon monoxide in a typical adult. The CFK model has been used to support discussions of the health effects of carbon monoxide in the ATSDR Toxicological Profile for carbon monoxide, by providing a means for interconverting carbon monoxide exposure levels expressed in units of ppm or mg/m<sup>3</sup> and corresponding equivalent steady-state COHb% values (i.e., the COHb% that would be achieved with continuous exposure to the reported air carbon monoxide concentration. (<http://www.atsdr.cdc.gov/ToxProfiles/tp201-c2.pdf>)

**Tuesday, September 13, 2011****Question:**

With regard to the potential for occupational exposure to manganese, what occupations may pose the greatest risk?

**Answer:**

The cited reference notes that the primary source of manganese exposure in humans is due to occupational exposure in miners, smelters, welders and workers in dry-cell battery factories. (Aschner M, et al. Manganese: Recent advances in understanding its transport and neurotoxicity. 2007 Tox and Applied Pharm, 221:131147)

**Monday, September 12, 2011****Question:**

What is the so-called fetal solvent syndrome?

**Answer:**

It is important to note that there is controversy regarding the existence of a fetal solvent syndrome- also called toluene embryopathy by some. However, the term fetal solvent syndrome has been applied to a constellation of morphological and behavioral effects that may result from extremely high levels of maternal solvent exposure; typically secondary to solvent abuse during the prenatal period. This may be associated with perinatal death and surviving neonates may be premature with growth retardation and microcephaly with severe facial dysmorphism (e.g., deep-set eyes, small face, low set ears, micrognathia), and spatulate fingertips and small fingernails. (Bowen SE and Hannigan JH. Developmental Toxicity of Prenatal Exposure to Toluene, 2006 The AAPS Journal, 8(2): E419-E424)

**Friday, September 9, 2011****Question:**

What is itai-itai disease?

**Answer:**

Itai-itai disease (translates literally from Japanese to: it hurts, it hurts or Ouch-Ouch) is a bone disease associated with fractures and severe pain. This disorder was identified after World War II in Japan and includes osteomalacia with increased serum levels of alkaline phosphatase and decreases in calcium and phosphate. Anemia and gastrointestinal and renal dysfunction can be associated as well. Eventually cadmium (usually as an environmental contaminant in food) was identified as the putative toxicant for this disorder. (Nordberg GF. Historical perspectives on cadmium toxicology. 2009 Tox Appl Pharm 238:192-200)

**Thursday, September 8, 2011****Question:**

What landmark U.S. Supreme Court case addressed the question: can women of child-bearing age be legally banned from working at a job or job task wherein a potentially fetotoxic agent was/is used?

**Answer:**

This landmark case was: INTERNATIONAL UNION, UNITED AUTOMOBILE, AEROSPACE & AGRICULTURAL IMPLEMENT WORKERS OF AMERICA, UAW, et al. v. JOHNSON CONTROLS, INC. (Justices for the Court: Harry A. Blackmun, Anthony Kennedy, Thurgood Marshall, Sandra Day O'Connor, Chief Justice William H. Rehnquist, Antonin Scalia, David H. Souter, John Paul Stevens, Byron R. White. Justices Dissenting: None. Date of Decision: March 20, 1991) The ultimate ruling was against Johnson Controls, Inc. by finding that their fetal protection policy (which prevented females of child bearing age from working in/around lead processes) violated Title VII of the Civil Rights Act of 1964 as amended by the Pregnancy Discrimination Act)

**Wednesday, September 7, 2011****Question:**

What are the most common infectious complications associated with the use of black tar heroin?

**Answer:**

Clostridial infections, including wound botulism, tetanus, and necrotizing fasciitis as well as polymicrobial infections and Staph aureus (including MRSA) infections and are the most common infectious complications associated with the use of black tar heroin. (Dunbar NM, et al. Necrotizing Fasciitis: Manifestations, Microbiology and Connection with Black Tar Heroin. 2007 J Forensic Sci. 52(4):920-923)

**Tuesday, September 6, 2011****Question:**

What is the principle toxin contained in the mushroom Amanita phalloides and what is its primary mechanism of action?

**Answer:**

The principle cyclo-peptide of toxicologic significance contained in the Amanita phalloides mushroom is alpha-amanitin. This chemical acts as a potent inhibitor of RNA polymerase II. (French LK, et al. Amanita phalloides poisoning. 2011 Clin Tox 49(2):128-129)

**Monday, September 5, 2011****Question:**

The practice known as chasing the dragon involves inhaling heroin vapors after heating the free base form of heroin. Typically, heroin is placed on foil above an open flame and the vapors produced are inhaled. What specific agent within the heroin vapors causes the rare form of toxic leukoencephalopathy associated with this practice? What are the typical imaging findings associated with this form of toxic leukoencephalopathy?

**Answer:**

The cited reference points out that a number of authors have postulated the causative agent in this instance to be an occasional contaminant that is activated by the heating of heroin. However no such specific agent has ever been identified. The imaging findings reported by the cited reference include low computed tomography attenuation and high T2 MRI signal most commonly in the posterior cerebral and cerebellar white matter, cerebellar peduncles, corpus callosum, and posterior limb of the internal capsules. In addition, there is often selective, symmetric involvement of the corticospinal tract, the medial lemniscus, and the tracts solitaires. (Hagel J, et al. Chasing the dragon-imaging of heroin inhalation leukoencephalopathy. 2005 Canadian Association of Radiologists Journal, 56(4):199-203)

**Friday, September 2, 2011****Question:**

Is there a role for the use of doxycycline in the treatment of pulmonary injury secondary to sulfur mustard exposure?

**Answer:**

There are actually multiple potential therapeutic interventions that may be considered to treat sulfur mustard related pulmonary toxicity. The cited reference points out doxycycline has been reported to exhibit non-specific MMP (matrix metalloproteinase) inhibitory activity, and it appears to exert significant protective effects against sulfur mustard-induced lung toxicity in experimental animals. The authors go on to indicate that in addition to inhibiting MMPs, doxycycline and related tetracyclines have been reported to attenuate iNOS expression and nitric oxide production, to reduce inflammatory cytokine release, and to scavenge reactive oxygen species. It is likely that these diverse anti-inflammatory actions enhance its (doxycycline) efficacy as a therapeutic against SM poisoning. (Weinberger B, et al. Sulfur mustard-induced pulmonary injury: Therapeutic approaches to mitigating toxicity, 2011 Pulm Pharm Ther 24(1):92-99)

**Thursday, September 1, 2011****Question:**

The nucleoside reverse transcriptase inhibitors zidovudine, didanosine, zalcitabine, stavudine, lamivudine, abacavir and tenofovir are pro-drugs that have been reported to manifest important toxicities. What are the toxicities that have been associated with this group of medications?

**Answer:**

Lactic acidosis with hepatic steatosis, fat atrophy, neuropathy, motor weakness, myositis, pancreatitis, aphthous ulcers, mitochondrial toxicity and bone marrow toxicity have all been reported in association with the use of these drugs. (Murphy RL. Defining the toxicity profile of nevirapine and other antiretroviral drugs. 2003 J Acquired Immune Def Syndromes, 34: S15-20)

**Wednesday, August 31, 2011****Question:**

Skin necrosis is pathognomonic for what complication of anti-coagulant therapy?

**Answer:**

Skin necrosis is pathognomonic for heparin induced thrombocytopenia. (Olah Z, et al. Coagulation: cascade!. 2011 The Lancet 378(9792):740)

**Tuesday, August 30, 2011****Question:**

Meperidine has been widely used as an analgesic. Patients with renal impairment receiving meperidine are at risk for specific toxicity. What is that toxicity and what is the basis for that toxicity?

**Answer:**

In healthy individuals meperidine is metabolized to an inactive compound, meperidinic acid, via hepatic carboxylase. Meperidine is also converted to normeperidine (the only metabolite of meperidine with significant pharmacologic activity). The plasma half-life of meperidine is 3 to 7 hours in both normal individuals as well as those with renal failure. However the plasma half-life of normeperidine increases from 14 to 21 hours in healthy individuals to 35 hours in those with significant renal impairment. The cited reference indicates normeperidine may thus accumulate in individuals with renal impairment and thus lead to a variety of neurotoxic problems including hallucinations, delirium, psychosis, tremor, clonus and seizures. (Hassan H, et al. Successful treatment of normeperidine neurotoxicity by hemodialysis. 2000 Am J Kidney Dis, 35(1): 146-149)

**Monday, August 29, 2011****Question:**

The anthracyclines are a group of cytotoxic antibiotics used as anti-cancer agents. The group includes doxorubicin (trade name Adriamycin), daunorubicin, epirubicin, idarubicin, and mitoxantrone. These compounds have demonstrated a serious irreversible and dose-limiting toxicity. What is that toxicity?

**Answer:**

Anthracyclines have been associated with irreversible cardiac damage (often manifesting clinically as congestive heart failure) as a major dose-limiting toxicity. The cardiac toxicity commonly limits the lifetime cumulative dose for these agents. (Fatima N, et al. Assessing adriamycin-induced early cardiotoxicity by estimating left ventricular ejection fraction using technetium-99m multiple-gated acquisition scan and echocardiography. 2011 Nuc Med Communications, 32:381-385)

**Friday, August 26, 2011****Question:**

Tetracyclines are contraindicated in pregnancy because they cross the human placenta and can have important adverse effects on the developing fetus. What are these potential adverse fetal effects?

**Answer:**

Tetracycline effects on the developing fetus may include discoloration of teeth, hypoplasia of the dental enamel and up to a 40 percent depression of bone growth. (Sanchez AR, et al. Tetracycline and other tetracycline-derivative staining of the teeth and oral cavity. 2004 Int J Dermatology, 43:709-715)

**Thursday, August 25, 2011****Question:**

What is CHEMTREC?

**Answer:**

CHEMTREC, stands for Chemical Transportation Emergency Center. CHEMTREC was established as a public service of the American Chemistry Council (ACC) in 1970 in order to provide a system to provide chemical specific information to emergency responders on a 24-hour basis. (<http://www.chemtrec.com/about/ACC/Pages/default.aspx>)

**Wednesday, August 24, 2011****Question:**

Secondary pneumatosis cystoides intestinalis (gas in the bowel wall) has been associated with a variety of clinical problems including COPD, bowel obstruction, necrotizing gastrointestinal infections and certain immunosuppressed conditions. What drug has been known to cause this condition?

**Answer:**

The use of alpha-glucosidase inhibitors (e.g. acarbose or miglitol) has been associated with the development of pneumatosis cystoides intestinalis. The cited reference points out that it is postulated that gas produced by the fermentation of excess luminal carbohydrate somehow enters the tissues of the bowel wall to cause this condition. (Image Challenge. 2011 NEJM web version at <http://www.nejm.org/>)

**Tuesday, August 23, 2011****Question:**

How does marijuana use in adolescents vary between states with medical marijuana laws compared with those states with no such legislation.

**Answer:**

Between 2002 and 2008, one study reports adolescent use of marijuana as being higher and perception of risk lower in states with medical marijuana laws compared with those states with no such legislation. (Wall MM, et al. Adolescent marijuana use from 2002 to 2008: Higher in states with medical marijuana laws, cause still unclear, 2011 Ann Epidemiol 21(9):714-716)

**Monday, August 22, 2011****Question:**

A 21-year-old Asian male presents to the ED with complaints of inability to walk or move his lower extremities. He has been abusing thyroid hormone he purchased on the Internet to help him control his weight. His initial serum potassium was reported to be 1.2 mEq/L. What is the most likely diagnosis?

**Answer:**

The likely diagnosis is thyrotoxic periodic paralysis or TPP. TPP is a disease characterized by episodes of paralysis (typically involving the lower extremities) and low serum potassium in the setting of thyrotoxicosis. The disease primarily affects individuals of Asian descent. (Diedrich DA and Wedel DJ. 2006 J Clin Anesth, 18:286-292)

**Friday, August 19, 2011****Question:**

Recent intelligence reports suggest that Al Qaeda's Yemeni branch may be seeking castor beans for making ricin. American counter-terrorism officials are increasingly concerned that the most dangerous regional arm of Al Qaeda is trying to produce the lethal poison ricin, to be packed around small explosives for attacks against the United States. (source ProMed ([www.promedmail.org](http://www.promedmail.org)), Ricin-International Bioterrorism Alert; August 16,2011) What is the ricin content of castor beans?

**Answer:**

Reports regarding the ricin content of castor beans vary but it probably is in the range of 1% to 5%. (Balint GA. Ricin: the toxic protein of castor oil seeds. Toxicology. 1974;2:77-102; Bradberry SM, et al. Ricin poisoning. Toxicol Rev. 2003;22:65-70 as cited in Audi J et al. Ricin poisoning: a comprehensive review. 2005 JAMA, 294(18):2342-2351)

**Thursday, August 18, 2011****Question:**

The clinical use of BOTOX by injection is generally considered to be safe and effective for a variety of medical problems. What is the complication of most concern associated with the use of BOTOX?



**Answer:**

The cited reference indicates that the greatest concern with the use of BOTOX involves formation of blocking antibodies leading to nonresponse of subsequent BOTOX injections. The only consequence is that BOTOX no longer is effective as a treatment. Prevalence of BOTOX resistance is less than 5% and is probably associated with dose and frequency of treatments as opposed to duration of the treatment regime.. (Klein AW. Complications and adverse reactions with the use of botulinum toxin. 2002 Disease-a-Month, 48:336-356)

**Wednesday, August 17, 2011****Question:**

Domoic acid is a neurotoxin produced by a variety of diatoms of the genus Pseudo-nitzschia and is responsible for an illness known as amnesic shellfish poisoning. This neurotoxic illness was first reported in 1987 when four people died and more than 140 were sickened following consumption of domoic acid-contaminated mussels harvested on the eastern coast of Prince Edward Island, Canada. What are the clinical signs associated with amnesic shellfish poisoning?

**Answer:**

The clinical signs of amnesic shellfish poisoning may include gastrointestinal distress, altered metal status, confusion, disorientation, memory loss, coma and, in the most severe cases, death. (Lefebvre KA and Robertson A. Domoic acid and human exposure risks: A review. 2010 Toxicol 56:281-230)

**Tuesday, August 16, 2011****Question:**

What is the role of the gastrointestinal iron transporter, divalent metal transporter 1 (DMT1), with regard to the relationship between blood lead status and iron status in children and infants?

**Answer:**

The relationship between lead and iron status depends, to a large extent, on a gastrointestinal iron transporter, divalent metal transporter 1 (DMT1). The authors of the cited study point out that DMT1 transports both iron and lead and that iron deficiency "increases DMT1 expression causing enhanced absorption of both iron and lead. Adequate iron intake inhibits lead absorption by decreasing DMT1 expression and also competitively inhibiting lead uptake by DMT1." (Chaparro CM et al. Early umbilical cord clamping contributes to elevated blood lead levels among infants with higher lead exposure. 2007 J Pediatr 151:506-512)

**Monday, August 15, 2011****Question:**

Is there a role for electroconvulsive therapy (ECT) in the treatment of neuroleptic malignant syndrome (NMS)?

**Answer:**

The authors of the cited paper point out that ECT has been advocated as a treatment for NMS, given that it may be effective in a variety of catatonic states. ECT may be effective even late in the course of NMS or in cases refractory to supportive care and pharmacotherapy. ECT may be preferred if idiopathic lethal catatonia cannot be excluded, if NMS symptoms are refractory to other measures, in patients with prominent catatonic features, and in patients who develop a residual catatonic-parkinsonian state or remain psychotic after NMS has resolved. It is important to recognize however that ECT has not been approved for use in NMS compared with the simple withdrawal of inciting agents and supportive care. (Campbell EC, et al. Neuroleptic malignant syndrome in elderly patients. 2007 Expert rev of Neurother, 7.4 (April):423)

**Friday, August 12, 2011****Question:**

What key factors may alter post mortem drug concentrations?

**Answer:**

Factors that may alter post mortem drug concentrations include: 1-time and circumstances of death; 2-site and timing of blood sampling; 3-diffusion of from body cavities; 4- redistribution; 5-metabolism, and 6-synthesis. (Kennedy M.C. Post-mortem drug concentrations. 2010 Int Med J 40:183-187)

**Thursday, August 11, 2011****Question:**

What are the most common riot control agents, what is the primary clinical effect of these chemicals and what clinical syndrome is associated with exposure to these agents?

**Answer:**

Chloroacetophenone (CN), chlorobenzylidenemalononitrile (CS), chloropicrin (PS), bromobenzylcyanide (CA), dibenzoxazepine (CR), and combinations of these chemicals are irritant agents that belong to a class of agents collectively known as riot control agents or tear gas. Although CN and CS are the most commonly used agents, many other tear gas agents have been used worldwide. Most exposures are inhalational, ocular, or dermal and typically lead to complaints of eye, nose, and throat irritation; hacking cough; suffocation or choking sensation; and dyspnea. Although unlikely, high-dose exposures in an enclosed space may lead to the development of airway edema, noncardiogenic pulmonary edema, and possibly respiratory arrest. (<http://emergency.cdc.gov/agent/riotcontrol/agentpoisoning.asp>)

**Wednesday, August 10, 2011****Question:**

What is "Syrian rue" and what are the potentially harmful chemicals contained therein?

**Answer:**

"Syrian rue" is Peganum harmala, a plant native to countries bordering the Mediterranean sea and in the western USA. The active constituents in this plant are harmaline, harmine and harmene, chemicals that exhibit varying degrees of inhibition of monoamine oxidase. (Yuruktumen A, et al. Syrian rue tea: A recipe for disaster. 2008 Clin Tox, 46(8):749-752)

**Tuesday, August 9, 2011****Question:**

What is the putative toxin associated with the blue-ringed octopus (Hapalochlaena sp)? What is characteristic of the bite of this marine animal and what situation is pathognomonic of the bite of the blue ringed octopus?

**Answer:**

The toxin associated with the blue-ringed octopus is tetrodotoxin, a sodium channel-blocking chemical. The bite of this animal is typically painless and the pathognomonic situation is collapse with paralysis, on or near a beach, shortly after a minor bite. (Cavazonni E, et al. Blue-ringed octopus (Hapalochaena sp.) envenomation of a 4-year old boy: A case report. 2008 Clin Tox 46(8):760-761)

**Monday, August 8, 2011****Question:**

PRES or posterior reversible encephalopathy syndrome is characterized by confusion, headache, altered mental status, seizures, and visual disturbances in conjunction with MRI findings consistent with vasogenic edema especially involving the occipito-parietal areas of the brain. The use of which drugs has been implicated in the development of PRES?

**Answer:**

PRES has been associated with the use of immunosuppressant agents and certain chemotherapeutic drugs as well as a variety of medical conditions including sepsis, autoimmune disease, renal disease, eclampsia, and hypertensive encephalopathy. The cited article posits that PRES may also be related to the use of nitrite containing inhalants. (Casetta I, et al. An acutely confused young woman. 2011 The Lancet, 378(9789):456)

**Friday, August 5, 2011****Question:**

Methamphetamine is easily produced in small illegal laboratories using potentially dangerous and readily available chemicals. Meth labs have been found in a variety of locations including homes, outbuildings, motels, and cars among other locales. Where do most clandestine meth lab related chemical spill/release events take place?

**Answer:**

Data from the Agency for Toxic Substances and Disease Registry's Hazardous Substances Emergency Events Surveillance (HSEES) Program indicate that the majority of clandestine meth lab events occurred in residential areas. About 15% of meth lab events required evacuation. Nearly one-fourth of these events resulted in injuries, with 902 reported victims. Most victims (61%) were official responders, and one-third were members of the general public. (Melnikova N, et al. Hazards of Illicit Methamphetamine Production and Efforts at Reduction: Data from the Hazardous Substances Emergency Events Surveillance System. 2011 Public Health Reports, 126 Suppl1: 116-123)



**Thursday, August 4, 2011**

**Question:**

The plant *Lophophora williamsii* has quite a storied past (and present). What is this plant and what is the potentially harmful chemical contained therein?

**Answer:**

*Lophophora williamsii* is peyote. The plant is a cactus containing the hallucinogen mescaline [2-(3,4,5-trimethoxyphenyl)ethanamine] and is found primarily in the southwestern US and northern Mexico. The authors of the cited reference point out that the dried tops of the plant (buttons) have been used for hundreds of years by Native Americans in religious ceremonies. (Carstairs SD and Cantrell FL. Peyote and mescaline exposures: a 12 year review of a statewide poison center database. 2010 Clin Tox 48(4):350-353)

**Wednesday, August 3, 2011**

**Question:**

What chemical, used as a chemical weapon during WWI, is sometimes called carbonyl chloride or carbonic acid dichloride and is a colorless non-flammable gas at normal pressure and temperature and reacts with human tissue by both acylation and hydrolysis.

**Answer:**

The chemical described above is phosgene. (Grainge C and Rice P. Management of phosgene-induced acute lung injury. 2010 Clin Tox 48(6):497-508)

**Tuesday, August 2, 2011**

**Question:**

What is the reported latent period between dermal exposure to sulfur mustard and the development of clinical signs and symptoms?

**Answer:**

The development of clinical signs and symptoms following dermal exposure to sulfur mustard may be delayed from 2 to 24 hours. (Carroll LS. Sulfur mustard: cutaneous exposure. 2005 Clin Tox 43(1):55)

**Monday, August 1, 2011**

**Question:**

What are the mechanisms of cardio and neuro-toxicity of *Aconitum* alkaloids?

**Answer:**

The cardiotoxicity and neurotoxicity of aconitine alkaloids are due to actions on voltage sensitive sodium channels of cell membranes of excitable tissue including in myocardium, nerve, and muscle. The cited reference indicates aconitine and mesaconitine bind with high affinity to the open state of the voltage-sensitive sodium channels at site 2, thereby causing a persistent activation of the channels by blocking their inactivation. Due to continuing sodium influx and sustained depolarization, the sodium channels become refractory to excitation. (Chan TYK. Aconite poisoning. 2009 Clin Tox 47(4):279-285)

**Friday, July 29, 2011**

**Question:**

What is salvarsan?

**Answer:**

Salvarsan was an organo-arsenical drug, first introduced by Paul Ehrlich in 1910. This drug, also known as "Ehrlich 606" or simply "606" was the 606th compound tested by Ehrlich in a search for a medication to treat syphilis. Salvarsan was used as an anti-syphilitic for many years before being abandoned for newer, more effective, and less harmful antibiotic medicines. (Bosch F and Rosich L. The contributions of Paul Ehrlich to pharmacology. 2008 Pharmacology 82:171-179)

**Thursday, July 28, 2011**

**Question:**

There are only a very limited number (probably about 20) cases of encephalopathy possibly related to the use of the drug metronidazole reported in the English language literature. What is the proposed pathophysiology for this admittedly rare event?

**Answer:**

The cited article reports that the specific pathophysiology for a metronidazole related encephalopathy is unknown but may be related to axonal swelling when doses of the drug exceed 2 grams daily for prolonged periods. The authors point out that this encephalopathy may be completely reversible after discontinuing the drug. (Khodakaram K and Barmano N. Uncommon reaction to a common prescription. 2011 The Lancet 378(9787):288)

**Wednesday, July 27, 2011**

**Question:**

What are the characteristics of the neuropathy that may arise in some cases of chronic exposure to n-hexane? What is the prognosis for n-hexane related neuropathy?

**Answer:**

The cited reference indicates that chronic n-hexane exposure produces a gradual sensorimotor neuropathy with demyelinating features. The most common initial complaint is numbness and tingling of the toes and fingers; a progressive loss of motor function may develop. Chronic polyneuropathy with demyelinating features also is associated with other underlying conditions. Other causes of peripheral neuropathy should be considered when evaluating persons with possible n-hexane-related peripheral neuropathy. Removal from n-hexane exposure is the only known treatment for n-hexane-related neurotoxicity. The prognosis for n-hexane neuropathy generally is favorable, but recovery may take months to years, depending on disease severity. (n-hexane- related peripheral neuropathy among automotive technicians California, 1999-2000, 2001 MMWR, 50(45):1011-1013)

**Tuesday, July 26, 2011**

**Question:**

Temperature related dysesthesia (unpleasant, abnormal sensations due to hot or cold temperatures) is a characteristic finding in most patients diagnosed with ciguatera fish poisoning. What other marine related toxicity may also manifest temperature related dysesthesia?

**Answer:**

NSP ( neurotoxic shellfish poisoning ) caused by ingestion of shellfish contaminated with the toxin known as brevetoxin may also manifest temperature related dysesthesia. (Friedman M, et al. Ciguatera fish poisoning: treatment prevention and management. 2008 Marine Drugs, 6:456-479)

**Monday, July 25, 2011**

**Question:**

What is subacute myelo-optic neuropathy also known as SMON? The use of what drug was implicated as causative of a large number of cases of SMON in Japan in the 1950s?

**Answer:**

SMON was identified in Japan in the 1950s and consisted of a constellation of symptoms including numbness, pain and intestinal distress progressing to paralysis and blindness. Cloquinoxol, an agent that acts as a mild metal chelator for copper, zinc and iron, was widely used in Japan as an anti-diarrheal over-the counter- drug and has been reported as the cause for SMON in some instances. Cloquinoxol overuse is associated with a black-green discoloration of the tongue. (Cahoon L. The curious case of cloquinoxol. Nature Medicine 15(4):356-359)

**Friday, July 22, 2011**

**Question:**

What is the Jarisch-Herxheimer reaction (JHR) and which patients are most susceptible to the development of this reaction?

**Answer:**

JHRs have been reported in individuals receiving certain antibiotics (including tetracyclines, penicillins, bismuth, and sulfonamides) for treatment of a variety of spirochetal illnesses such as Lyme disease, leptospirosis, yaws, syphilis. JHR can occur as early as 2 hours after the first antibiotic dose with resolution usually complete by 24 hours. Patients may manifest fever and rigors, followed by diaphoresis as well as headache, myalgias and general malaise. Interestingly, the signs and symptoms of the treated disease may actually worsen during the course of any JHR. Jarisch-Herxheimer reactions have been reported more frequently in HIV infected patients. (See S et al. Penicillin-Induced JarischHerxheimer Reaction. 2005 Anns Pharmacotherapy, 39:2128-2130)

**Thursday, July 21, 2011**

**Question:**

Methyl bromide is a colorless and odorless chemical that has been used as a fumigant and has been associated with disabling neurologic symptoms including ataxia, dizziness and memory problems). The use of methyl bromide was strictly limited in 2005. What limitations were placed on the use of this chemical?

**Answer:**

Most use of methyl bromide stopped by 2005 but its use is still permissible to treat commodities potentially contaminated with a recognized quarantine pest and to treat certain agricultural items (e.g. soil and seedlings) when no feasible alternative exists. (<http://www.epa.gov/opp00001/reregistration/REDS/methylbromide-red.pdf> as quoted in MMWR Illness associated with exposures to methyl bromide 60(27):923-926)

**Wednesday, July 20, 2011****Question:**

What class of drugs is responsible for the most common cause of secondary osteoporosis?

**Answer:**

Glucocorticoid therapy is the most common cause of secondary osteoporosis. Often, the presenting manifestation is fracture, which occurs in 30 to 50% of patients receiving long-term glucocorticoid therapy. (Weinstein RS. Glucocorticoid-induced bone disease 2011 NEJM; 365:62-70)

**Tuesday, July 19, 2011****Question:**

Botulism is caused by a paralyzing toxin produced by Clostridium botulinum bacteria. Heating food can inactivate the botulinum toxin. To what temperature and for what duration must food be heated in order to inactivate the toxin?

**Answer:**

Botulinum toxin can be inactivated by heating food to 185°F (85°C) for 5 minutes. (Notes from the Field: Botulism Caused by Consumption of Commercially Produced Potato Soups Stored Improperly --- Ohio and Georgia, July 8, 2011 MMWR, 60(26); 890)

**Monday, July 18, 2011****Question:**

Tendon rupture is a recognized phenomenon reportedly related to the use of fluoroquinolones. What is the incidence of tendon rupture related to fluoroquinolone use and which patients taking these drugs are at increased risk of suffering tendon rupture? Is the incidence of tendon rupture more likely for those taking levofloxacin as compared with other fluoroquinolones?

**Answer:**

The incidence of tendon rupture related to fluoroquinolone use is reported to be in the range of 1 in 6000. The risk of tendon rupture associated with fluoroquinolone use is increased in those older than 60 years of age, those taking steroids and in patients who have received heart, renal, or pulmonary transplants. There is no evidence that tendon rupture is more likely for patients taking levofloxacin (The Medical Letter, 53(1368):55-56)

**Friday, July 15, 2011****Question:**

What conditions may be associated with the development of yellow palms and soles?

**Answer:**

Yellow palms and soles can occur with hypothyroidism, diabetes mellitus, and carotenemia. The discoloration may be associated with end products of advanced glycation. (Image challenge. <http://www.nejm.org>, accessed July 13, 2011)

**Thursday, July 14, 2011****Question:**

What is the cause for the musty, earthy odors sometimes associated with the presence of indoor mold growth?

**Answer:**

So-called microbial volatile organic compounds (MVOCs) cause the musty, earthy odors associated with mold growth. The perception of these odors does not constitute exposure to mold and there is no association between these odors and the development of any mold related medical problem. (Horner E., et al. Guide for interpreting reports from inspections/ investigations of indoor mold. 2008 J Allergy Clin Immunol 2008;121:592-597)

**Wednesday, July 13, 2011****Question:**

The American Heart Association recommends individuals with coronary disease consume 1 gram of EPA and DHA per day from oily fish or fish oil capsules. What is the current caution that must be taken with regard to fish oil capsules and the presence of methyl mercury that may exist in fish oil capsules?

**Answer:**

The commercial fish oil supplements tested to date have been free of methylmercury and thus this is not a serious concern. (De Caterina R. n-3 fatty acids in cardiovascular disease. 2011 NEJM 364(25):2439-2450)

**Monday, July 11, 2011****Question:**

What is the relationship between long-term use of bisphosphonates (BPs) and sub-trochanteric and femoral shaft fractures?

**Answer:**

The cited reference points out that BPs are highly effective at reducing the risk of spine and non-spine fractures, including typical and common femoral neck and intertrochanteric fractures. However, there is evidence of a relationship between long-term BP use and a specific type of sub-trochanteric and femoral shaft fracture. These fractures are characterized by unique radiographic features (i.e., transverse or short oblique orientation, absence of comminution, cortical thickening, stress fracture or stress reaction on the symptomatic and/or contralateral side, and delayed healing) and unique clinical features (i.e., prodromal pain and bilaterality. Despite the suggested association, the cited reference emphasizes more information is urgently needed both to assist in identifying patients at particular risk and to guide decision making about duration of BP therapy. (Shane E, et al. Atypical Subtrochanteric and Diaphyseal Femoral Fractures: Report of a Task Force of the American Society for Bone and Mineral Research. 2010 J Bone Min Research 25(11):2267-2294)

**Friday, July 8, 2011****Question:**

Etanercept is a tumor necrosis factor alpha antagonist. The use of this agent has been associated with an increased risk for the development of infections with which organisms?

**Answer:**

Treatment with the TNF-alpha antagonist etanercept has been associated with a slightly increased risk of infection by both common and unusual organisms. In particular, there is a higher risk of bacterial infections (e.g., with listeria, nocardia, or various mycobacteria) that are associated with granulomatous host responses. Morris A. et al. A Sleeping Giant 2011 N EJM, 365:72-77)

**Thursday, July 7, 2011****Question:**

Gun bluing solution is a commercially available material used to impart a gun-metal, blue-black luster to metal (usually firearms) What are the chemical constituents of gun bluing solution?

**Answer:**

The cited reference points out that most gun-bluing agents contain formulations in the range of 2-9% selenious acid and 2-4% copper(II) in dilute acid. While gun-bluing agents may contain relatively high concentrations of copper the toxicity related to ingestion of this material is primarily related to selenium. (Nuttall KL. Review: evaluating selenium poisoning. 2006 Anns Clin Lab Sci, 36(4): 409-420)

**Wednesday, July 6, 2011**

**Question:**

Envenomations by which arthropods have been reported to be associated with elevations of cardiac troponins reflecting myocardial injury usually in the absence of coronary artery occlusion?

**Answer:**

Envenomation by black widow spiders, centipedes, and scorpions, has been reported as a source of elevated cardiac troponins reflecting myocardial injury usually in the absence of coronary artery occlusion. (Kelley WE, et al. Increases of cardiac troponin in conditions other than acute coronary syndrome and heart failure. 2009 Clinical Chemistry 55(12): 2098-2112)

**Tuesday, July 5, 2011**

**Question:**

The ingestion of what common substance may interfere with the successful reversion of paroxysmal supraventricular tachycardia (SVT) by the use of adenosine? Why?

**Answer:**

Caffeine is an adenosine receptor blocker and should, theoretically, reduce adenosine efficacy in the treatment of paroxysmal supraventricular tachycardia (SVT). The cited reference reported that ingestion of caffeine less than 4 hours before a 6-mg adenosine bolus significantly reduced its effectiveness in the treatment of SVT. The authors suggest that an increased initial adenosine dose may be indicated for these patients. (Cabalg MS et al. Recent caffeine ingestion reduces adenosine efficacy in the treatment of paroxysmal supraventricular tachycardia. 2009 Academic Emerg Med, 17 (1):44-49)

**Friday, July 1, 2011**

**Question:**

What is konzo?

**Answer:**

The cited reference indicates that konzo is a disorder characterized by the sudden onset of irreversible spastic paraparesis, associated with prolonged high dietary cyanogenic glucoside consumption and a diet deficient in sulphur amino acids. The cyanogenic glucosides originate from insufficiently processed roots of bitter cassava. Cassava is a staple root used in many under-developed countries. (Cliff J. et al. Konzo and continuing cyanide intoxication from cassava in Mozambique. 2011 Food and Chemical Toxicology 49: 631-635)

**Thursday, June 30, 2011**

**Question:**

Optic neuritis has been reported to be an important consequence of thallium poisoning. What is the prevalence of optic neuritis in thallium poisoning?

**Answer:**

Severe bilateral optic neuritis is reported in roughly 25% of acute thallium poisoning cases and in virtually all cases of chronic poisoning. (Pelcova D., et al. Two-year follow-up of two patients after severe thallium intoxication. 2009 Human & Experimental Toxicology 28: 263-272)

**Wednesday, June 29, 2011**

**Question:**

What is Thorotrast and what adverse health effects have been associated with exposure to this substance?

**Answer:**

Thorotrast is a 25% colloidal solution of thorium dioxide that was used on a world wide basis as a contrast agent in angiography and other radiological studies from 1930 through the mid 1950s. A variety of cancers have been associated with exposure to Thorotrast. The most common cancers reportedly associated with this agent are hepatic neoplasms including primary hepatocellular carcinoma and hepatic angiosarcoma. (Lee F, et al. Malignant hepatic tumors associated with previous exposure to Thorotrast: four cases. 1996 Eur J Gastro & Hepatology, 8:1121-1124)

**Tuesday, June 28, 2011**

**Question:**

Levamisole is an antihelmintic drug specifically formulated for veterinary applications. Levamisole has recently become recognized as an additive in illicit cocaine purportedly used to enhance the euphoric effects of cocaine. When should a clinician consider the possibility that a patient has used cocaine contaminated with levamisole?

**Answer:**

The cited reference notes that levamisole toxicity resulting from the use of adulterated cocaine may be an increasing problem and should be considered in a cocaine user with neutropenia and reticular purpura. (Trevor T., et al. Toxic effects of levamisole in a cocaine user. 2011 NEJM 364:e52 June 16, 2011)

**Monday, June 27, 2011**

**Question:**

What is JP-8 and what are the most common routes for human exposure to JP-8?

**Answer:**

JP-8 is Jet Propulsion Fuel 8 and is the standard fuel for military aircraft. In addition, JP-8 is used as a fuel for a variety of military appliances and engines and as a coolant in certain types of engines. Using one single fuel for a variety of applications substantially simplifies military supply and logistics. Some have indicated that JP-8 may be the most common source for chemical exposures that may occur on military bases worldwide. The most common potential routes of exposures to JP-8 are dermal and inhalational. (Kim D. Dermal absorption and penetration of jet fuel components in humans. 2006 Tox Letters, 165:11-21)

**Friday, June 24, 2011**

**Question:**

What are the clinical characteristics of envenomation by the Gaboon viper (*Bitis gabonica*)?

**Answer:**

The primary clinical findings include rapid onset of swelling and extreme pain at the site of the bite with bleeding and hemorrhagic edema at the bite site. In addition, difficulty breathing and loss of consciousness with hematuria, hematemesis, and local tissue necrosis may be prominent findings. Despite these very serious clinical manifestations, the cited reference notes: Despite this bleak picture, recovery after antivenom is usually complete and uncomplicated. (Marsh N, et al. Gaboon viper (*Bitis gabonica*) envenomation resulting from captive specimens A review of five cases. 2007 Clin Tox 45 (1):60-64)

**Thursday, June 23, 2011**

**Question:**

How can the diagnosis of berylliosis (chronic beryllium disease) be confirmed?

**Answer:**

The cited reference points out that the diagnosis of chronic beryllium disease can be confirmed by the presence of granuloma on tissue biopsy and evidence that the granuloma was caused by a hypersensitivity to beryllium using the beryllium lymphocyte proliferation test (BeLPT). The BeLPT can be performed on cells derived from blood or a bronchoalveolar lavage (BAL). However, it is important to note that a positive BeLPT, can occur in the absence of granulomatous disease in tissues. (Santo Tomas LH. Beryllium hypersensitivity and chronic beryllium lung disease. 2009 Current Opinion in Pulmonary Medicine, 15:165169)

**Wednesday, June 22, 2011**

**Question:**

For how long should consumption of locally grown produce and groundwater be avoided or curtailed following an accident where iodine-131 has been released?

**Answer:**

The half-life of iodine-131 is eight (8) days. Consequently, the consumption of locally grown produce and groundwater would not be expected to contain substantial amounts of iodine-131 after 8-12 weeks following a single exposure source release. (Christodouleas JP, et al. Short-Term and Long-Term Health Risks of Nuclear-Power-Plant Accidents. 2011 NEJM 364:2334-2341)

**Tuesday, June 21, 2011**

**Question:**

It is well known that coal miners inhale varying amounts of coal dust while working. When these exposures are large and lung clearance is overwhelmed, over time, dust particles accumulate causing a reduction in airflow associated with the development of interstitial disease. This is known as coal workers pneumoconiosis (CWP). A related disorder is known as progressive massive fibrosis (PMF). What exactly is PMF?

**Answer:**

PMF, also known as complicated pneumoconiosis, occurs when fibrotic nodules of CWP (as well as other pneumoconiosis such as those related to silica) coalesce and expand forming lesions measuring more than 10 mm on chest x-ray. (Wade WA, et al, Severe occupational pneumoconiosis among West Virginia coal miners. 2011 Chest, 139(6):1458-1462)

**Monday, June 20, 2011****Question:**

Chronic use of metformin has been associated with deficiency of what vitamin? In what percentage of long term metformin users will this vitamin deficiency be seen? What diagnostic confusion might this phenomenon result in?

**Answer:**

Chronic metformin use results in vitamin B12 deficiency in up to 30% of patients. Vitamin B12 deficiency, which may present without anemia and as a peripheral neuropathy, is often misdiagnosed as diabetic neuropathy, although the clinical findings are usually different. Failure to diagnose the cause of the neuropathy will result in progression of central and/or peripheral neuronal damage which can be arrested but not reversed with vitamin B12 replacement. (Bell DS. Metformin-induced vitamin B 12 deficiency presenting as a peripheral neuropathy. 2010 So Med J. 103(3):265-267)

**Friday, June 17, 2011****Question:**

Agent Orange is the best-known herbicide defoliant used during the Vietnam War however a number of other herbicide defoliants were also used during that war. One such defoliant was known as Agent Blue. What was the active component of Agent Blue?

**Answer:**

The active component of Agent Blue was an arsenic-containing compound, cacodylic acid (hydroxydimethyl arsine oxide). (Young AL, et al. Environmental fate and bioavailability of Agent Orange and its associated dioxin during the Vietnam War. 2004 Environ Sci & Pollut Res, 11(6):359-370)

**Thursday, June 16, 2011****Question:**

An emergency physician wishes to treat a firefighter found unconscious on a fire ground empirically for cyanide toxicity but the pharmacy states they do not have hydroxocobalamin (or thiosulfate) available. The pharmacist instead recommends the use of vitamin B 12. Why is this advice seriously flawed?

**Answer:**

The cited reference points out that hydroxocobalamin (vitamin B12a), the natural form of vitamin B12, is a hemelike molecule containing a complexed cobalt (Co) atom. Hydroxocobalamin acts as a cyanide antidote by direct binding to cyanide to form nontoxic cyanocobalamin that is excreted in the urine. Vitamin B 12 itself does not complex with cyanide nor does it increase the excretion of cyanide. Thus it does not act in the same way that hydroxocobalamin does. (Hall A, et al. Sodium Thiosulfate or Hydroxocobalamin for the Empiric Treatment of Cyanide Poisoning. 2007 Ann Emerg Med 49(6):806-813)

**Wednesday, June 15, 2011****Question:**

What is the purpose for, and what are the components of, the so-called King criteria?

**Answer:**

The King criteria were developed to predict the likelihood of death from fulminant liver failure associated with APAP ingestion. The King criteria are: 1- serum pH less than 7.3 after adequate fluid resuscitation, 2- creatinine greater than 3.3 mg/dL, 3- INR higher than 6.5, and 4- grade III or grade IV encephalopathy. (Eanes KM and Burgess BE. 2011 Critical Decisions in Emerg Med. 25(7):2-8)

**Tuesday, June 14, 2011****Question:**

Niacin is commonly used in the management of dyslipidemia however intense flushing associated with this therapy is an important reason for the discontinuation of therapy, estimated at rates as high as 25% 40%. What is the mechanism for niacin-induced flushing?

**Answer:**

The cited reference indicates that niacin-induced flushing appears to be due to the subcutaneous release of PGD2, which is mediated by niacin's action as a pharmacologic ligand for the adipocyte and macrophage G protein coupled nicotinic acid receptor GPR109A and appears to involve the formation of various prostanoids with vasodilator effects. (Davidson M. Niacin use and cutaneous flushing: Mechanisms and strategies for prevention. 2008 Am J Cardiol 101[suppl]:14B19B) 101[suppl]:14B19B)

**Monday, June 13, 2011****Question:**

The Tobacco Products Scientific Advisory Committee (TPSAC) of the Food and Drug Administration recently released its report on menthol-containing cigarettes. While this report did not indicate that the addition of menthol to cigarettes increases toxicity, the report does point out several important potentially adverse effects of menthol in cigarettes. What are these effects?

**Answer:**

The TPSAC report concluded that menthol masks the harshness of tobacco, making cigarettes more appealing, especially to young people who might otherwise be deterred by irritation or an unpleasant taste. The report also concluded that smokers of menthol cigarettes have a more difficult time quitting than smokers of nonmenthol cigarettes. (Siegel M. A lost opportunity for public health-The FDA advisory committee report in menthol. 2011 NEJM 364:2177-2179. June 9, 2011)

**Friday, June 10, 2011****Question:**

What is the material that has become known as "Libby asbestos"?

**Answer:**

In the 1970s and 1980s, the medical community noted elevated rates of asbestos-related lung diseases among vermiculite miners in Libby, Montana. In the late 1990s, the EPA and the ATSDR became involved in the investigation and determined that the vermiculite mined in the Libby, Montana, area was contaminated with tremolite, actinolite, as well as other forms of amphibole asbestos. This has become known as Libby asbestos. (Goldyn SR, et al. The burden of exposure-related diffuse lung disease. 2008 Seminars in Resp Crit Care Med, 29(6):591-602)

**Thursday, June 9, 2011****Question:**

Fish gallbladder has long been used as a folk remedy in the Far East and India and in recent years in the United States. The gallbladder of many fish species contains a toxic element. What is that potentially harmful compound and what are the target organs for toxicity in humans?

**Answer:**

Fish gallbladder contains 5 alpha cyprinol sulphate, a 27 carbon bile salt, which may be both hepatotoxic and nephrotoxic to humans. (Kung SW, et al. Acute renal failure and hepatitis following ingestion of carp gallbladder. 2008 Clin Tox 46(8):753-757)

**Wednesday, June 8, 2011****Question:**

What is the Widmark equation?

**Answer:**

The Widmark equation is a basic equation used to estimate the amount of alcohol consumed. The cited reference points out that important uncertainty is inherent in the Widmark formula and these uncertainties should be discussed whenever alcohol estimates are derived using this formula. (Gullberg RG. Estimating the uncertainty associated with Widmark's equation as commonly applied in forensic toxicology. 2007 For Sci International 172:33-39)

**Tuesday, June 7, 2011**

**Question:**

What is the Pliofilm cohort?

**Answer:**

The Pliofilm cohort was a cohort of workers exposed to benzene during the manufacture of Pliofilm, a glossy membrane made from rubber hydrochloride and used primarily for packaging and other water resistant applications. This cohort was studied to develop estimates of the benzene related risk of leukemia. The risk assessment that derived from this cohort was used by OSHA to support the reduction of the permissible exposure limit (PEL) for benzene from 10 ppm to 1 ppm. (Crump K. Risk of benzene-induced leukemia predicted from the Pliofilm cohort. 1996 Env Health Pers. 104 (Supple 6):1437-1441)

**Monday, June 6, 2011**

**Question:**

What is glyphosate? What is the mechanism of action for this chemical in its intended commercial use?

**Answer:**

Glyphosate (marketed under the trade name of Roundup and Zero Weed Killer among other names) is generally marketed as a combination of polyoxyethylene amine surfactant and glyphosate as an isopropyl- ammonium salt. It is currently the most commonly used post-emergent non-selective herbicide used the United States. Glyphosate is absorbed into plants in a process facilitated by the surfactant and the glyphosate targets the synthesis of chlorophyll-related molecules by competitive inhibition of the enzyme enolpyruvylshikimate phosphate synthase, an enzyme present in plants but not in animals. (Moon J and Jo Chun B. Predicting acute complicated glyphosate intoxication in the emergency department. 2010 Clin Tox 48(7):718-724)

**Friday, June 3, 2011**

**Question:**

In utero exposure to the synthetic non-steroidal estrogen, diethylstilbestrol (DES), in the past, was associated with the development of a rare vaginal clear-cell adenocarcinoma (CCA). What is the median age at which CCA appeared in those women who were exposed to DES in utero?

**Answer:**

CCA in DES-exposed women occurred at a median age of 19 years (range, 15 to 29 years) (Goodman A et al. The long term effects of in utero exposures-The DES story. 2011 NEJM, 364:2083-2084)

**Thursday, June 2, 2011**

**Question:**

What are the most common clinical effects associated with occupational exposure to platinum salts?

**Answer:**

Platinum salts have been associated with an increased incidence of asthma, rhinoconjunctivitis and dermatitis and urticaria among workers occupationally exposed to these metals such as those in catalyst production and refineries. (Wiseman CLS and Zereini F. 2009 Sci Tot Env, 407:2493-2500)

**Wednesday, June 1, 2011**

**Question:**

What are the most common adverse clinical effects of the substances known as "bath salts"?

**Answer:**

According to a recent report from the Michigan Dept of Community Health and the Children's Hospital of Michigan Poison Control Center the most common signs and symptoms of toxicity related to "bath salts" were agitation (66%), tachycardia (63%), and delusions/hallucinations (40%) (MMWR, May 20, 2011, 69(19):624-627)

**Tuesday, May 31, 2011**

**Question:**

Industrial exposure to vinyl chloride monomer (VCM) has been associated, in some circumstances, with the development of what clinical problems?

**Answer:**

The cited reference points out that VCM is causally associated with the development of a form of non-cirrhotic portal hypertension related to sinusoidal endothelial damage, and to angiosarcoma of the liver. More recently it has been suggested that VCM may cause hepatocellular carcinoma. (Sherman M. Vinyl chloride and the liver. 2009 J Hepatology, 51:1074-1081)

**Monday, May 30, 2011**

**Question:**

An increasing body of literature suggests that cadmium may be an important risk factor for cardiovascular morbidity and mortality. What is the relationship between blood cadmium levels and blood pressure?

**Answer:**

The cited reference reports the body of evidence relating blood cadmium levels to BP suggests a positive relationship, especially in females, but in the absence of doseresponse gradients in individuals who have never smoked is inconclusive. (Gallagher C and Meliker J. Blood and Urine Cadmium, Blood Pressure, and Hypertension: A Systematic Review and Meta-analysis. 2010 Env Health Persp, 118 (12):1676-1684)

**Friday, May 27, 2011**

**Question:**

What is kratom?

**Answer:**

Kratom, (*Mitragyna speciosa* korth), is a tropical tree indigenous to Thailand, Malaysia, Myanmar and other areas of South East Asia. Traditionally, kratom was used as a stimulant by Thai and Malaysian laborers and farmers to overcome the burdens of hard work. They chewed the leaves to make them work harder and provide energy and relief from muscle strains. Kratom was also used in Southeast Asia and by Thai natives to substitute for opium when opium is not available. It has also been used to manage opioid withdrawal symptoms by chronic opioid users. Known as "herbal speedball" in the UK, kratom is abused in the USA as an herbal tea or by chewing the plant leaves ([http://www.deadiversion.usdoj.gov/drugs\\_concern/kratom.htm](http://www.deadiversion.usdoj.gov/drugs_concern/kratom.htm))

**Thursday, May 26, 2011**

**Question:**

How is *Salvia divinorum* classified under the Federal Controlled Substances Act?

**Answer:**

*Salvia divinorum* and salvinorin A are not currently controlled under the CSA. However, a number of states have placed controls on *Salvia divinorum* and/or salvinorin A. ([http://www.justice.gov/dea/concern/salvia\\_divinorum.html](http://www.justice.gov/dea/concern/salvia_divinorum.html))

**Wednesday, May 25, 2011**

**Question:**

Why is the vitreous humor (VH) often used for post mortem drug testing?

**Answer:**

The vitreous is often used because it appears to be less susceptible than blood to postmortem redistributive changes. The cited reference notes that it is also a more simple environment than putrefied blood, containing 9899% water. The reference states that VH may be the best substrate for measurement of postmortem drug concentrations "if the body has undergone considerable bleeding, decomposition, or burning". (Yarema MS and Becker C. Key Concepts in Postmortem Drug Redistribution. 2005 Clin Tox. 43:235-241)

**Tuesday, May 24, 2011**

**Question:**

How does one tell the difference between water hemlock (*Cicuta* spp) and poison hemlock (*Conium maculatum*) on a clinical basis after ingestion as well as for identification in the field?

**Answer:**

The cited reference notes "*Cicuta* spp causes seizures and potentially status epilepticus where as *Conium maculatum* results in respiratory paralysis, secondary to muscle weakness. The two plants can also be distinguished on the basis of their characteristic morphological properties: *Conium maculatum* has a single tap root, purple and spotted stem, while *Cicuta* spp. have branched root systems with tubules and an absence of purple spots." (Scheep LJ, et al. Poisoning due to water hemlock. 2009 Clin Tox 47:270-278)

**Monday, May 23, 2011**

**Question:**

The European yew (*Taxus baccata*) contains two toxins; taxine A and taxine B. What is the primary toxicity of taxine B?

**Answer:**

Taxine B is cardiotoxic with manifestations similar to class I antiarrhythmic agents as well as calcium channel blocking effects. (Soumagne N, et al. Treatment of yew leaf intoxication with extracorporeal circulation. 2011 Am J Emerg Med 29; 354-355)

**Friday, May 20, 2011**

**Question:**

What is Medwatch?

**Answer:**

MedWatch is the FDA Safety Information and Adverse Event Reporting Program. More information regarding Medwatch can be found at: <http://www.fda.gov/Safety/MedWatch>

**Thursday, May 19, 2011**

**Question:**

FDA has approved pentetate calcium trisodium injection (Calcium-DTPA) and pentetate zinc trisodium injection (Zinc-DTPA) to treat people internally contaminated with what three substances?

**Answer:**

FDA has approved pentetate calcium trisodium injection (Calcium-DTPA) and pentetate zinc trisodium injection (Zinc-DTPA) to treat people internally contaminated with plutonium, americium, or curium. (<http://www.fda.gov/Drugs/EmergencyPreparedness/Bioterrorism/DrugPreparedness/ucm130311.htm>)

**Wednesday, May 18, 2011**

**Question:**

Methotrexate is a commonly prescribed antineoplastic and immune modulating compound often used in the management of rheumatoid arthritis, psoriasis, sarcoidosis and a number of neoplastic disorders. Pulmonary toxicity related to methotrexate is commonly seen. What is the most common manifestation of methotrexate pulmonary toxicity?

**Answer:**

Pulmonary infiltrates are the most commonly encountered form of methotrexate pulmonary toxicity. The cited reference notes that these infiltrates may resemble hypersensitivity lung disease. Lateef O, et al. Methotrexate pulmonary toxicity. 2005 Expert Opinion on Drug Safety 4(4): 723-730

**Tuesday, May 17, 2011**

**Question:**

In food-borne botulism there appears to be an association between toxin type and the rate of recovery. Which sero-type of food borne botulism is associated with the most rapid recovery of neuromuscular junction function?

**Answer:**

The neuromuscular junction recovers most rapidly with type B intoxications. (Thompson JA, et al. Infant botulism in the age of botulism immune globulin. 2005 Neurology 64:2029-2032)

**Monday, May 16, 2011**

**Question:**

What causes the majority of cases of infant botulism in the United States?

**Answer:**

The cited reference points out that while infants may acquire spores from a variety of food sources, contamination of the gastrointestinal tract by ingestion of dust from environmental sources containing *C botulinum* spores causes the majority of cases of infant botulism in the United States. (Thompson JA, et al. Infant botulism in the age of botulism immune globulin. 2005 Neurology 64:2029-2032)

**Friday, May 13, 2011**

**Question:**

What is the most common etiology for allergic contact dermatitis related to clothing?

**Answer:**

The most common etiology for allergic contact dermatitis related to clothing actually involves the chemicals used in the manufacture of the clothing as opposed to the actual clothing fibers themselves. (Aldrich SL, et al. Permanent press allergy in an active duty US Army soldier. 2011 Mil Med, 176(5):584-585)

**Thursday, May 12, 2011**

**Question:**

Quercetin (3,3',4',5',7-pentahydroxyflavone) is a naturally occurring flavonol that purportedly has antioxidant, anti-inflammatory, anti-carcinogenic and cardio-protective effects. What is the effect of this flavonol on energy, fatigue and sleep quality?

**Answer:**

A recent study of healthy male and female military personnel reports that taking quercetin supplementation for six weeks had no influence on energy levels, level of fatigue, or sleep quality. (Bigelman K. et al. Effects of 6 weeks of quercetin supplementation on energy, fatigue and sleep in ROTC cadets. 2011 Mil Med 176(5):565-572)

**Wednesday, May 11, 2011**

**Question:**

What is "critical illness polyneuropathy" (CIP)?

**Answer:**

CIP is a complication of severe critical illness and its management. The precise pathophysiology of "critical illness polyneuropathy" has not yet been elucidated however CIP is associated with prolonged mechanical ventilation, increased ICU and hospital length of stay as well as increased mortality. Some authors have speculated that this problem may be related to overly aggressive use of neuromuscular blocking agents but other theories also exist. (Hermans G, et al. Clinical review: critical illness polyneuropathy and myopathy. 2008 Crit Care, 12(6):238-247)

**Tuesday, May 10, 2011**

**Question:**

What are the signs and symptoms associated with organophosphate-induced delayed polyneuropathy (OPIDP)?

**Answer:**

The signs and symptoms associated with OPIDP include tingling of the hands and feet, followed by sensory loss, progressive muscle weakness and flaccidity of the distal skeletal muscles of the lower and upper extremities, as well as ataxia. (Costa LG. Current issues in organophosphate toxicology. 2006 Clinica Chimica Acta 366: 1-13)

**Monday, May 9, 2011**

**Question:**

What does the acronym ALARA stand for?

**Answer:**

ALARA stands for "as low as reasonably achievable" and is a terminology most often used in relation to radiation exposure levels, designating a work principle or philosophy intended to protect workers from unnecessary exposure to workplace hazards. (MMWR, April 15,2011, Supplement Vol 60. page7)

**Friday, May 6, 2011**

**Question:**

The FDA has recently approved a transdermal patch formulation for the partial opioid agonist buprenorphine (Butrans). What are the most frequently reported adverse effects of transdermal buprenorphine per clinical trials of this new formulation?

**Answer:**

The most frequently reported adverse effects of transdermal buprenorphine are nausea, vomiting, dizziness, headache, somnolence and constipation. (The Medical Letter, April 18,2011, 53(1362):31-32)

**Thursday, May 5, 2011**

**Question:**

Long term infusions with lorazepam have been associated with an increased risk for toxicity from a specific chemical. What is that chemical?

**Answer:**

Propylene glycol used as a diluent for lorazepam has been associated with an increased risk for toxicity when lorazepam has been administered as a long term intravenous infusion. (Wood S and Winters ME. Care of the intubated ED patient. 2011 J Emerg Med, 40(4):419-427)

**Wednesday, May 4, 2011**

**Question:**

Some patients with renal insufficiency may have prolonged sedation from midazolam. What is the explanation for this phenomenon?

**Answer:**

Patients with renal insufficiency may suffer prolonged sedation from midazolam due to the accumulation of the active metabolite of midazolam, 1-hydroxylmethylmidazolam. (Wood S and Winters ME. Care of the intubated ED patient. 2011 J Emerg Med, 40(4):419-427)

**Tuesday, May 3, 2011**

**Question:**

Ingestion of what toxicant results in green nails?

**Answer:**

The answer is that no specific exogenous toxicant has been reported to cause green nails. The cited reference reports green nails may result from bacterial infection with *P. aeruginosa* and is usually seen in patients with nail disease such as onycholysis, onychotillomania, or paronychia. This occurs more commonly in patients whose abnormal nails have been exposed to moist environments. The green color is caused by the fluorescent siderophore pyoverdine, produced by *P. aeruginosa*. (Hengge UR and Bardeli V. Green nails. 2009 NEJM 360:1125)

**Monday, May 2, 2011**

**Question:**

What is thebaine?

**Answer:**

Thebaine is a minor constituent of opium and is controlled in Schedule II of the CSA as well as under international law. Although chemically similar to both morphine and codeine, thebaine produces stimulatory rather than depressant effects. Thebaine is not used therapeutically, but is converted into a variety of substances including oxycodone, oxymorphone, nalbuphine, naloxone, naltrexone, and buprenorphine. The United States ranks first in the world in thebaine utilization. (<http://www.justice.gov/dea/pubs/abuse/doa-p.pdf>)

**Friday, April 29, 2011**

**Question:**

Microvascular steatosis (MS) is a condition caused by impairment of mitochondrial function in which decreased fatty acid beta oxidation results in the accumulation of free fatty acids and triacylglycerol. What are the potential toxicological causes for MS?

**Answer:**

Microvascular steatosis has been associated with aspirin (in Reyes syndrome), valproate, nucleoside analogues (e.g. didanosine and zidovudine), MDMA, tetracycline, *Bacillus cereus* emetic toxin, acute iron overload and/or acute iron toxicity. (Fearing MK, et al. Case 12-2011: A 9 month-old boy with acute liver failure. 2011 NEJM 364(16):1545-1556)

**Thursday, April 28, 2011**

**Question:**

What form of tobacco use has been recently described by the American Lung Association as "an emerging deadly trend"? This form of tobacco use has been found to be possibly associated with lung and esophageal cancer, as well as low birth weight and periodontal disease.

**Answer:**

Water pipe smoking is the form of tobacco use recently described by the American Lung Association as "an emerging deadly trend". (Raad D, et al. Effects of water pipe smoking on lung function. 2011 Chest,139(4):764-774)

**Wednesday, April 27, 2011**

**Question:**

What is (was) "fire gilding"?

**Answer:**

Fire gilding was an extremely hazardous process used to apply gold coatings to art and decorative statuary by the application of mercury/gold mixtures to the surface of the statuary followed by heating with fire. This volatilized the mercury and left the gold adhered to the surface. Unfortunately workers then inhaled large quantities of mercury with all of the inherent associated toxicities. This process was used for thousands of years until the late 1800's. (Oddy A. Gilding through the ages. 1981 Gold Bulletin 14(2):75-79)

**Tuesday, April 26, 2011**

**Question:**

What are the three most common adverse drug events due to the drug amphotericin B?

**Answer:**

The three most common adverse drug events due to the drug amphotericin B are 1-infusion related reactions, 2-liver toxicity, and 3-renal toxicity. (Patel, et al, An evaluation of hepatotoxicity and nephrotoxicity of liposomal amphotericin B (L-AMB) 2011 J Med Tox 7(1):12-15)

**Monday, April 25, 2011**

**Question:**

Polyvalent crotalidae antivenin is derived from the venom of four (4) different snake species. What are they?

**Answer:**

Polyvalent crotalidae antivenin is derived from the venom of four (4) different snake species: 1- western diamondback (*Crotalus atrox*), 2-fer-de-lance (*Bothrops atrox*), 3- South American rattlesnake (*C. durissus terrificus*), 4- eastern diamondback rattlesnake (*Crotalus adamanteus*). (Lynch M, et al. Successful treatment of South American rattlesnake envenomation with crotalidae polyvalent immune fab. 2011 J Med Tox 7(1):44-46)



**Friday, April 22, 2011**

**Question:**

What is acid rain?

**Answer:**

"Acid rain" is a broad term referring to a mixture of wet and dry deposition (deposited material) from the atmosphere containing higher than normal amounts of nitric and sulfuric acids. The precursors of acid rain formation result from both natural sources, such as volcanoes and decaying vegetation, and man-made sources, primarily emissions of sulfur dioxide (SO<sub>2</sub>) and nitrogen oxides (NO<sub>x</sub>) resulting from fossil fuel combustion. (<http://www.epa.gov/acidrain/what/index.html>)

**Thursday, April 21, 2011**

**Question:**

What are the potential illicit uses for human growth hormone?

**Answer:**

Human growth hormone is illicitly used as an anti-aging agent, to improve athletic performance, and for bodybuilding purposes. It is marketed, distributed, and illegally prescribed off-label to aging adults to replenish declining hGH levels and reverse age-related bodily deterioration. It is also abused for its ability to alter body composition by reducing body fat and increasing skeletal muscle mass. It is often used in combination with other performance enhancing drugs, such as anabolic steroids. Athletes also use it to improve their athletic performance, although the ability of hGH to increase athletic performance is debatable. ([http://www.deadiversion.usdoj.gov/drugs\\_concern/hgh.htm](http://www.deadiversion.usdoj.gov/drugs_concern/hgh.htm))

**Wednesday, April 20, 2011**

**Question:**

What is Philopon and Sedrin?

**Answer:**

Philopon and Sedron are two formulations of methamphetamine that were sold over the counter in Japan in the early 1940s. These compounds were specifically advertised to fight sleepiness and enhance vitality. (Anglin MD, et al. History of the Methamphetamine Problem. 2000 J Psychoactive Drugs, 32(2):137-141)

**Tuesday, April 19, 2011**

**Question:**

The primary hallucinogenic chemical found in Cannabis sativa is delta 9-tetrahydrocannabinol (THC). THC is subject to hepatic metabolism primarily by hydroxylation. What is the primary metabolite of THC and what enzyme mediates its formation?

**Answer:**

The primary metabolite is 11-hydroxy-THC (HO-THC), which is pharmacologically active, and is formed by CYP2C9. (Maurer HH, et al. Toxicokinetics of Drugs of Abuse: Current Knowledge of the Isoenzymes Involved in the Human Metabolism of Tetrahydrocannabinol, Cocaine, Heroin, Morphine, and Codeine. 2006 Ther Drug Monit, 28:447-453)

**Monday, April 18, 2011**

**Question:**

What effect does tobacco smoke have on the progression of diabetic neuropathy?

**Answer:**

Using a diabetic mouse model, researchers from the University of Alabama at Birmingham report that exposure to tobacco smoke worsens the progression of diabetic nephropathy, likely mediated by increased expression of profibrotic cytokines. (Obert DM, et al. Environmental tobacco smoke furthers progression of diabetic nephropathy. 2011 Am J Med Sci 341(2):126-130)

**Friday, April 15, 2011**

**Question:**

An intravenous preparation of acetaminophen (Ofirmev) has been approved by the FDA to treat pain and/or fever. How does the maximum serum concentration of acetaminophen following intravenous administration compare with the same dose administered orally?

**Answer:**

The maximum serum concentrations of acetaminophen following IV administration are approximately 70% higher than those associated with the same dose given orally. (The Medical Letter, April 4, 2011, 53(1361):27)

**Thursday, April 14, 2011**

**Question:**

An FDA warning has noted that the prolonged use of proton pump inhibitor drugs (PPI's) can result in hypomagnesemia. What is believed to be the mechanism for this effect?

**Answer:**

While the exact mechanism is yet to be elucidated, the cited reference points out that in some patients, PPIs appear to interfere with active transport of magnesium across the intestinal wall or cause excessive loss of magnesium into the intestinal lumen. (The Medical Letter, April 4, 2011, 53(1361):25)

**Wednesday, April 13, 2011**

**Question:**

In the event of exposure to radioactive iodine, recommendations for treatment may include the administration of potassium iodide (KI) in order to block thyroid uptake of radioactive iodine. What is the degree of protection afforded by this drug in relation to time of exposure?

**Answer:**

Taken within 12 hours before exposure, KI is expected to prevent virtually 100% of uptake. After exposure however, the degree of protection falls to 80% after 2 hours, 40% after 8 hours, and 7% after 24 hours. (The Medical Letter, April 4, 2011, 53(1361):25-26)

**Tuesday, April 12, 2011**

**Question:**

Currently, there are three (3) prescription products available containing non-selective cannabinoid agonists. What are these three drugs and what is each used for clinically?

**Answer:**

These three agents are nabilone (Cesamet®), dronabinol (Marinol®), and delta-9-THC/cannabidiol (Sativex®) are currently available clinically for use as antiemetics, appetite stimulants, and analgesics. (Seely KA, et al. Marijuana-based drugs: innovative therapeutics or designer drugs of abuse? 2011 Molecular Interventions 11(1): 36-51)

**Monday, April 11, 2011**

**Question:**

Hydroxocobalamin for parenteral treatment of cyanide toxicity must be reconstituted before use. What is the recommended diluent for this purpose?

**Answer:**

The recommended diluent is 0.9% sodium chloride however Ringers lactate and 5% dextrose have also been found to be compatible with hydroxocobalamin and may be used if 0.9% NaCl is not available. (package insert for Cyanokit; Meridian Medical Technologies, 2011)

**Friday, April 8, 2011**

**Question:**

What are the three chelating agents available for the treatment of iron overload due to chronic transfusion therapy?

**Answer:**

1-Deferoxamine is a siderophore produced by the bacterium Streptomyces pilosus; 2-Deferasirox is a synthetic chelating agent; 3- A third iron chelator, the synthetic oral agent deferiprone (Ferriprox, Apotex; Kelfer, Cipla), is not approved for use in the United States or Canada. (Brittenham GM. Iron-chelating therapy for transfusional iron overload. 2011 NEJM 364:146-156)



**Thursday, April 7, 2011**

**Question:**

What food/beverages increase the risk for gout? What food/beverages decrease the incident risk for gout?

**Answer:**

The risk for gout is increased in persons with an increased intake of dietary purines (particularly meat and seafood), ethanol (particularly beer and spirits), soft drinks, and fructose and is decreased in those with an increased intake of coffee, dairy products, and vitamin C (which lower urate levels) (Neogi T. Gout. 2011 NEJM 364(5): 443-452)

**Wednesday, April 6, 2011**

**Question:**

What is the current (and anticipated future) risk for radiation contamination of cows milk related to the ongoing Fukushima Daiichi nuclear plant disaster? What agency has jurisdiction over the safety, labeling and identity of milk and milk products in interstate commerce?

**Answer:**

According to the FDA website: EPA conducts radiological monitoring of milk under its RADNET program, while the U.S. Food and Drug Administration has jurisdiction over the safety, labeling and identity of milk and milk products in interstate commerce. States have jurisdiction over those facilities located within their territory. Results from a screening sample taken March 25 from Spokane, WA detected 0.8 pCi/L of iodine-131, which is more than 5,000 times lower than the Derived Intervention Level set by FDA. These types of findings are to be expected in the coming days and are far below levels of public health concern, including for infants and children. Iodine-131 has a very short half-life of approximately eight days, and the level detected in milk and milk products is therefore expected to drop relatively quickly. (<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm249146.htm>)

**Tuesday, April 5, 2011**

**Question:**

What complication is of primary concern for individuals with renal disease who receive gadolinium in conjunction with an MRI scan?

**Answer:**

Individuals with renal failure risk developing nephrogenic systemic fibrosis if they receive gadolinium when undergoing MRI scan. (Perazella MA. Current status of gadolinium toxicity in patients with kidney disease. 2009 Clin J Am Soc Nephrol 4: 461469)

**Monday, April 4, 2011**

**Question:**

How much epinephrine is delivered by the adult EpiPen autoinjector? How much is delivered via the device known as EpiPen Jr?

**Answer:**

The adult EpiPen auto-injector system delivers 0.3 mg of epinephrine (1:1000) in 0.3 cc. The pediatric EpiPen Jr device delivers 0.15 mg of epinephrine (1:2000) in 0.3 cc. (Greenberg MI and Rivello RJ. Local effects after inadvertent digital injection with an epinephrine auto-injector. 2010 Clin Tox 48(10):1179-1180)

**Friday, April 1, 2011**

**Question:**

How many venomous snakebites occur worldwide each year and how many result in death?

**Answer:**

The cited reference points out that the World Health Organization (WHO) estimates approximately 2,500,000 venomous snakebites per year result in 125,000 deaths worldwide, 100,000 of which are in Asia and approximately 20,000 in Africa. However, the true global incidence of envenomation and its severity remain largely misunderstood. Hospital-based data are likely to under-estimate the incidence, the case-fatality ratio, and the overall contribution snakebites make to worldwide morbidity and mortality because most victims seek traditional treatment; these victims may die at home and their deaths remain unrecorded. (Cruz L, et al. Snakebite envenomation and death in the developing world. 2009 Ethnicity & Disease, 19 [Suppl 1]:S1-42-S1-46)

**Thursday, March 31, 2011**

**Question:**

What is the most likely mechanism for toxicity in chloroquine poisoning?

**Answer:**

According to the cited reference, "chloroquine toxicity is attributed to sodium channel inhibition resulting in intraventricular conduction blockade, ventricular rhythm disturbances and cardiovascular collapse." (Megarbane B, et al. Blood concentrations are better predictors of chloroquine poisoning severity than plasma concentrations: a prospective study with modeling of the concentration/effect relationship. 2010 Clin Tox 48(9):904-915)

**Wednesday, March 30, 2011**

**Question:**

In the GI tract, botulinum toxin undergoes active transport across the lumen of the intestinal tract via endocytosis and transcytosis. Which botulinum serotypes are most efficiently transported across the intestinal lumen?

**Answer:**

Serotypes A and B are the most efficiently transported across the intestinal lumen. (Horowitz BZ. Type E botulism. 2010 Clin Tox 48(9):880-895)

**Tuesday, March 29, 2011**

**Question:**

Some experts have recommended CYP2C19 genotyping for certain patients taking clopidogrel. Why?

**Answer:**

A recent meta analysis of nine studies of clopidogrel involving more than 9600 patients who had an acute coronary syndrome or were undergoing percutaneous coronary intervention reported a significant association between the homozygous or heterozygous state for CYP2C19 reduced function alleles and an increased risk of death from cardiovascular causes, MI, or stroke. (Wang L, et al. Genomics and drug response. 2011 NEJM 364(12):1144-1153)

**Monday, March 28, 2011**

**Question:**

What do kiwifruit and latex have in common?

**Answer:**

Kiwifruit and latex share several antigens. Thus individuals who are allergic to either kiwifruit or latex may also suffer allergic reactions to the other material. (Murali MR, et al. Case 9-2011: A 37-year old man with flushing and hypotension. 2011 NEJM 364(12):1155-1165)

**Friday, March 25, 2011**

**Question:**

What is the difference between mild forms of carbamazepine hypersensitivity reactions and more severe reactions of carbamazepine hypersensitivity?

**Answer:**

Mild carbamazepine hypersensitivity reactions take the form of maculopapular exanthema and occur in 5-10 % of treated persons of European ancestry. This mild reaction tends to resolve when the drug is discontinued. More severe reactions can be life-threatening (n up to 10% of patients) and may include fever, rash, eosinophilia, hepatitis and nephritis. The most severe reactions include toxic epidermal necrolysis and Stevens Johnson syndrome. (McCormack M, et al. HLA-A\*3101 and carbamazepine-induced hypersensitivity reactions. in Europeans. 2011 NEJM 364(12):1134-1143)

**Thursday, March 24, 2011**

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**Question:**

What is the specific target for warfarin-based anticoagulants?

**Answer:**

The target for warfarin-based anticoagulants is vitamin K epoxide reductase complex subunit 1 (VKORC1). ( Wang L., et al. Genomics and drug response. 2011 NEJM 364(12):1144-1153)

**Wednesday, March 23, 2011****Question:**

Exposure to methylmercury from eating fish has been suggested by some to increase the risk of cardiovascular disease. How real is this risk?

**Answer:**

A recent study of more than 51,000 adult males and 121,000 adult females reported "no evidence of any clinically relevant adverse effects of mercury exposure on coronary heart disease, stroke, or total cardiovascular disease in US adults at the exposure levels seen in this study". (Mozaffarian D, et al. Mercury exposure and risk of cardiovascular disease in two U.S. cohorts. 2011 NEJM 364(12):1116-1125)

**Tuesday, March 22, 2011****Question:**

What is feverfew?

**Answer:**

Feverfew is a plant (Tanacetum parthenium) that has been recommended for its medicinal properties for centuries. Feverfew contains a series of compounds known as sesquiterpene lactones including the key compound parthenolide. Parthenolide reportedly exerts an anti-secretory effect on platelets, inhibiting the release of serotonin. This may form the mechanism for the anti-migraine effects attributed by some to feverfew. (Heptinstall S. Feverfew- an ancient remedy for modern times? 1988 J Royal Soc Medicine, 81:373-374)

**Monday, March 21, 2011****Question:**

What are the risk factors that predict ketamine-associated airway and respiratory adverse events?

**Answer:**

Risk factors that predict ketamine-associated airway and respiratory adverse events are high intravenous doses, administration to children younger than 2 years or aged 13 years or older, and the use of co-administered anticholinergics or benzodiazepines. (Green SM et al. Predictors of airway and respiratory adverse events with ketamine sedation in the emergency department: an individual-patient data meta-analysis of 8,282 children. 2009 Ann Emerg Med, 54(2):158-168)

**Friday, March 18, 2011****Question:**

Humans require only 2-8 minutes of summer sun exposure in order to maximize the synthesis of vitamin D3. Can sunscreen use result in insufficient production of vitamin D3?

**Answer:**

The cited reference indicates that it is "unlikely" that the use of sunscreens, used as directed, will result in inadequate production of vitamin D3. (March 7, 2011 The Medical Letter, 53(1359):18)

**Thursday, March 17, 2011****Question:**

The FDA has recently issued a warning regarding the drug Dronedarone (Multaq), an amiodarone analog. What was the basis for the concerns reflected in this FDA warning?

**Answer:**

Dronedarone was approved in 2009 for the treatment of atrial fibrillation. Since that time this drug has been reportedly associated with a number of cases of liver injury and hepatic failure with two cases requiring liver transplantation. (March 7, 2011 The Medical Letter, 53(1359):17)

**Wednesday, March 16, 2011****Question:**

Following the Chernobyl radiation incident what was the primary cause of death for those exposed persons who died within the first two months following the incident?

**Answer:**

Bone marrow failure was the main contributor to all deaths during the first 2 mo. (Mettler FA, et al. Health effects in those with acute radiation sickness from the Chernobyl accident. 2007 Health Physics, 93(5):462-469)

**Tuesday, March 15, 2011****Question:**

What are the clinical manifestations of acute radiation sickness?

**Answer:**

The major clinical manifestations of acute radiation sickness (ARS) are dependent upon the dose of radiation received. According to the cited reference, the major manifestations of ARS include signs of hematopoietic depression with concurrent infection and hemorrhage (hematopoietic syndrome). The intestinal, toxemia, and cerebral syndromes occur after large doses with signs of diarrhea, water loss, fever, arterial blood pressure drop, and changes of function and structure of the brain. Occasionally, with very high acute doses to the head or trunk, there may be loss of consciousness, which is sometimes referred to as transient incapacitation (or central nervous system) syndrome. (Mettler FA, et al. Health effects in those with acute radiation sickness from the Chernobyl accident. 2007 Health Physics, 93(5):462-469)

**Monday, March 14, 2011****Question:**

In 2008 a nationwide outbreak of salmonellosis occurred in the United States. What was the source for this extensive salmonella outbreak that affected 1500 individuals and caused the death of two people?

**Answer:**

The outbreak strain was identified in jalapeno peppers collected in Texas and in agricultural water and serrano peppers on a Mexican farm. (Behraves CB, et al. 2008 outbreak of salmonella Saintpaul infections associated with raw produce. 2011 NEJM 364(10):918-927)

**Friday, March 11, 2011****Question:**

The drug dapsone is a common etiology for acquired methemoglobinemia. What is the mechanism for the development of dapsone-induced methemoglobinemia?

**Answer:**

The cited reference reports that dapsone undergoes N-hydroxylation by various hepatic P-450 enzymes to form N-hydroxy dapsone. It is this hydroxylamine metabolite (N-hydroxy dapsone), and not the parent drug dapsone, that induces the formation of methemoglobinemia. N-hydroxy dapsone mediates the oxidation of the iron moiety of the heme molecule to produce methemoglobin in a dose dependent fashion. (Pallais JC, et al. Case 7-2011: A 52 year old man with upper respiratory symptoms and low oxygen saturation levels. 2011 NEJM 364(10): 957-966)

**Thursday, March 10, 2011****Question:**

Succinylcholine has a relatively short shelf life. What storage technique has been shown to prolong the shelf life of this drug?

**Answer:**

With refrigeration, succinylcholine maintains approximately 90% of its activity for approximately 90 days. (Mace S. Rapid sequence intubation. 2011 Critical Decisions in Emergency Medicine, 25(6):2-11)

**Wednesday, March 9, 2011**

**Question:**

What is MDPV?

**Answer:**

MDPV is 3,4-Methylenedioxypropylvalerone. It was first synthesized as part of a class of stimulants in 1969 and is the methylenedioxy analogue of pyrovalerone, a Schedule V stimulant first synthesized in 1964. Pyrovalerone, available under the trade names Centroton and Thymergix, is used as an appetite suppressant or for the treatment of chronic fatigue. This substance is found in a variety of products known as bath salts sold under a variety of names including Serenity Now, Ivory Wave, Vanilla Sky, Bonsai Grow, Lovey Dovey, Euphoria, White Lightening, Cloud 9, Aura, and Blue Silk. MDPV is currently unscheduled in the United States. (Yohannan JC and Bozenko JS. The characterization of 3,4-Methylenedioxypropylvalerone (MDPV) 2010 Microgram Journal, 7(1):12-15.)

**Tuesday, March 8, 2011**

**Question:**

Accidental inhalation of medically important doses of what chemical used in the production of yellow-green fireworks and can result in profound (K less than 2.0) hypokalemia? What is the mechanism for this profound hypokalemia?

**Answer:**

Accidental inhalation of soluble barium chloride used in manufacturing can result in profound hypokalemia, caused by inactivation of the passive potassium channels in the muscle cell membrane, thereby blocking efflux of intracellular potassium. Because activity of the adenosine triphosphatase sodium-potassium pump (Na<sup>+</sup>-K<sup>+</sup>-ATPase) is unchanged and continues to exchange sodium and potassium, potassium thus is trapped intracellularly. (Su Y, et al. 2010 American Journal of Kidney Diseases, 56(3): pp xxxviii-xli)

**Monday, March 7, 2011**

**Question:**

Plague is a category A potential bioterrorism agent caused by the organism *Yersinia pestis*. Human infections are rare but can be life-threatening. What is the case fatality rate for plague?

**Answer:**

The plague case fatality rate depends on the clinical presentation (i.e. bubonic, septicemic or pneumonic) and timing of antibiotic therapy initiation. If untreated, the case-fatality rate is in excess of 50% for bubonic plague and approaches 100% for pneumonic plague. (MMWR, 60(7):214)

**Friday, March 4, 2011**

**Question:**

What is the average half life of cocaine when used by inhalation (smoking, as opposed to insufflation)?

**Answer:**

The cited study reports the average half life of cocaine when used by inhalation (smoking) is between 38 and 39 minutes. Other studies have reported half lives closer to 60 minutes. (Isenschmid DS, et al. Concentrations of cocaine and metabolites in plasma of humans following intravenous administration and smoking of cocaine. 1992 J Analytical Tox 16:311-314)

**Thursday, March 3, 2011**

**Question:**

What is the epidemiology of foodborne illness in the United States today?

**Answer:**

The CDC now estimates that there are approximately 48 million foodborne illnesses, 128,000 hospitalizations, and 3000 deaths per year. That means that 15% of Americans can expect to have a foodborne illness annually and that 41 in 100,000 will be hospitalized and 1 in 100,000 will die (Osterholm MT. Foodborne Disease in 2011- The rest of the story. 2011 NEJM 364(8))

**Wednesday, March 2, 2011**

**Question:**

What is the effect of pregnancy on the rate of caffeine metabolism?

**Answer:**

During pregnancy, the rate of caffeine metabolism decreases progressively from the first to third trimester, with a doubling of the half-life of caffeine. (Maslova E, et al. Caffeine consumption during pregnancy and risk of preterm birth: a meta-analysis. 2010 Am J Clin Nutr, 92:112032)

**Tuesday, March 1, 2011**

**Question:**

What is erionite?

**Answer:**

Erionite is a naturally occurring fibrous mineral found in the volcanic tuffs, or soil in certain locations of the world including the Cappadocia region of Turkey. It belongs to a group of minerals called zeolites. Erionite is considered to be a nonasbestos mineral. Exposure to erionite has been associated with a high prevalence of mesothelioma in those regions of Turkey where this element exists. (Dikensoy O. Mesothelioma due to environmental exposure to erionite in Turkey. 2008 Current Opinion in Pulmonary Medicine, 14:322325)

**Monday, February 28, 2011**

**Question:**

What is the biological basis for the use of naloxone in some cases of hepatic encephalopathy?

**Answer:**

Plasma concentrations of some opioid peptides have been observed to be elevated in patients with both acute and chronic liver disease. Thus, it is possible that opioid peptides in the central nervous system are implicated in some of the manifestations of hepatic encephalopathy. (Jiang Q, et al Naloxone in the management of hepatic encephalopathy. 2-010 Journal of Clinical Pharmacy and Therapeutics, 35: 333341)

**Friday, February 25, 2011**

**Question:**

What is biomass smoke and the risk for what adverse health outcome is increased due to exposure to biomass smoke?

**Answer:**

Wood and other forms of biomass (animal dung, crop residues, and so forth) are commonly used as sources of energy in developing countries and are estimated to be used for 50% of household cooking and heating fuels worldwide. Combustion of biomass produces a large amount of smoke that spreads into the environment as air pollutants. Exposure to such biomass smoke has been documented as playing an important role in mortality and morbidity globally. The inhalation of biomass smoke is a risk factor for the development of COPD. (Hu G., et al. Risk of COPD from exposure to biomass smoke. 2010 Chest 138(1):

**Thursday, February 24, 2011**

**Question:**

What is TENORM and what is the hazard posed by these materials?

**Answer:**

Naturally occurring radioactive materials (NORM) are ubiquitous throughout the earth's crust. Human manipulation of NORM for economic ends, such as mining, ore processing, fossil fuel extraction, and commercial aviation, may lead to what is known as technologically enhanced naturally occurring radioactive materials, often called TENORM. The existence of TENORM results in an increased risk for human exposure to radioactivity. Workers in TENORM-producing industries may be occupationally exposed to ionizing radiation. (Vearrier D, et al. Technologically enhanced naturally occurring radioactive materials. 2009 Clin Tox 47(5):393-406)

**Wednesday, February 23, 2011**

**Question:**

What is a Biomonitoring Equivalent (BE)?

**Answer:**

A Biomonitoring Equivalent (BE) is defined as the concentration or range of concentrations of a chemical or its metabolites in a biological medium (blood, urine, or other medium) that is consistent with an existing health-based exposure guidance value such as a reference dose (rfd) or Tolerable Daily Intake (TDI). BE's can be estimated using available human or animal pharmacokinetic data. They are intended to be used as screening tools to provide assessment of which chemicals have large, small, or no margins of safety compared to existing risk assessments and exposure guidance values. (Hays SM, et al. Biomonitoring equivalents for inorganic arsenic. 2010 Reg Tox Pharm 58;1-9)

**Tuesday, February 22, 2011**

**Question:**

What is the mechanism of tissue necrosis associated with intranasal cocaine use?

**Answer:**

The cited reference points out the mechanism of tissue necrosis associated with intranasal cocaine use is probably related to vasoconstriction occurring as a result of sympathetic stimulation due to inhibition of epinephrine and norepinephrine reuptake. Cocaine may also induce local vasoconstriction by stimulation of vascular smooth muscle. Chronic vasoconstriction results in mucosal ischemia, atrophy and, at some point, then to necrosis. Finally, the substances that may be added to street cocaine such as talc, mannitol and etc., may act as mechanical and chemical irritants leading to giant cell granulomatous reactions that may be destructive to local tissue. (Greene D. Total necrosis of the intranasal structures and soft palate as a result of nasal inhalation of crushed oxycontin. 2005 ENT-Ear, Nose & throat Journal pp 512-516)

**Monday, February 21, 2011**

**Question:**

Smoking tobacco using a narghile waterpipe (shisha, hookah) is an extremely popular pursuit worldwide. Users are attracted by the highly aromatic and sweetened tobacco paste known as massel, which typically contains approximately 25 wt.% tobacco and a similar amount of glycerol. What are the potential important toxicological exposures for individuals who smoke tobacco products via the narghile waterpipe (shisha, hookah)

**Answer:**

Polycyclic aromatic hydrocarbons (PAHs) including benzo[a]pyrene, anthracene, naphthalene, and others as well as carbon monoxide are found in the mainstream and sidestream smoke generated by narghile water pipes. (Sepetdjian E, et al. Carcinogenic PAH in water pipe charcoal products. 2010 Food and Chemical Tox, 48: 3242-3245)

**Friday, February 18, 2011**

**Question:**

What is the mechanism by which etomidate is reported to cause adrenal suppression?

**Answer:**

Etomidate inhibits 11 $\beta$ -hydroxylase, an enzyme required for adrenal steroid production. Even after a single dose of etomidate, transient adrenal suppression has been reported although this limited effect is probably not clinically significant. (Mace S. Rapid sequence intubation. 2011 Critical Decisions in Emergency Medicine, 25(6):2-11)

**Thursday, February 17, 2011**

**Question:**

What is mesna?

**Answer:**

Mesna is sodium 2-mercaptoethanesulfonate and is widely used for the prevention of hemorrhagic cystitis resulting from cyclophosphamide administration and the ensuing production of oxazaphosphorine metabolites. (Khaw SL, et al. Adverse hypersensitivity reactions to mesna as adjunctive therapy for cyclophosphamide. 2005 Ped Blood Cancer, 49(3): 341-343)

**Wednesday, February 16, 2011**

**Question:**

Tobacco smoke is recognized as the most important cause for lung cancer. Is the susceptibility to develop lung cancer related to cigarette smoke the same for both males and females?

**Answer:**

According to the cited reference women appear to have increased susceptibility to tobacco carcinogens but have a lower rate of fatal outcome of lung cancer compared with men. This research reported the prevalence OR comparing women with men was 1.9 (95% confidence interval [CI], 1.5-2.5). However, the hazard ratio of fatal outcome of lung cancer comparing women with men was 0.48 (95% CI, 0.25-0.89) (Mitchell SL. Women's susceptibility to tobacco carcinogens and survival after diagnosis of lung cancer. 2006 JAMA 296(2):180-184)

**Tuesday, February 15, 2011**

**Question:**

A recent FDA warning indicated that the antitussive agent benzonatate (e.g. Tessalon Perles) could be hazardous for children under 10 years of age. What was the basis for this FDA warning?

**Answer:**

According to the FDA warning, overdose with benzonatate in children less than 2 years of age has been reported following accidental ingestion of as few as 1 or 2 capsules. Individuals who experience overdose of benzonatate may exhibit restlessness, tremors, convulsions, coma, and cardiac arrest. Signs and symptoms of overdose can occur rapidly after ingestion (within 15-20 minutes). Deaths in children have been reported within hours of the accidental ingestion. In addition, if the capsules are chewed, then release of benzonatate from the capsule in the mouth can produce a temporary numbing of the mouth and choking could occur. Finally, FDA points out the safety and effectiveness of benzonatate in children below the age of 10 years have not been established. Therefore, prescribing benzonatate to that age group is not recommended. (<http://www.fda.gov/drugs/drugsafety/ucm236651.htm> and February 7, 2011, The Medical Letter, 53(1357):9)

**Monday, February 14, 2011**

**Question:**

In January of 2008, Baxter Healthcare Corporation voluntarily recalled 9 lots of heparin due to reports of severe adverse events associated with these lots. What clinical issues were involved and what primary contaminant was discovered in these lots of heparin?

**Answer:**

The cited reference indicates The recall was due to a heterogeneous and complex report of severe adverse events (diarrhea, dizziness, dyspepsia, dyspnea to arrhythmia, flushing, headache, hyperthyroidism, hypoesthesia, increased lacrimation, loss of consciousness, malaise, nausea, pallor, palpitation, paresthesia, pharyngeal edema, restlessness, vomiting, stomach discomfort, tachycardia, thirst, trismus, unresponsiveness to stimuli, and drug ineffectiveness). In addition to 785 reports of the described symptoms, as many as 256 deaths may be linked to the use of these heparin lots. These multiple adverse reactions were later attributed to heparin manufactured by Baxters (Deerfield, Illinois) suppliers using raw material from China. Over-sulfated chondroitin sulfate (OSCS) was eventually identified in heparin preparations and considered the main contaminant. The precise source of the contamination is, to date, unknown. (Ramacciotti E, et al. Contaminants in heparin: review of the literature, molecular profiling, and clinical implications. Clin Appl Thromb Hemost. Published online 1 Feb 2011. Online version available at: <http://cat.sagepub.com/content/early/2011/01/28/1076029610392214>)

**Friday, February 11, 2011**

**Question:**

Yerba mate (Ilex paraguariensis) is used to create a popular tea ingested the world over. What are the risks for immunocompromised individuals who drink this tea, often recommended for its anti-oxidant and other potential alternative therapeutic effects?

**Answer:**

The cited study shows that the practice of drinking yerba mate infusion may be associated with the ingestion of potentially pathogenic fungi, in particular Aspergillus species. Some of these fungi were able to survive extreme variations in pH and temperature. Although more studies are needed to better clarify the inoculum required to cause disease in the vulnerable patient, it might be prudent to recommend that immunocompromised patients abstain from consuming yerba mate infusion. (Viera N, et al. Drinking yerba mate infusion: a potential risk factor for invasive fungal diseases? 2010 Transplant Infectious Disease 12(6):565-569)

**Thursday, February 10, 2011**

**Question:**

A number of animal studies suggest that nanomaterials may induce unique toxicities in vivo. What are the currently reported human toxicities associated with exposure to nanomaterials?

**Answer:**

The cited reference notes to date, there is no conclusive evidence of a known human toxic response that is specifically caused by nanomaterials. (Kim BY, et al. Nanomedicine. 2010 NEJM 363:2434-2443)

**Wednesday, February 9, 2011****Question:**

What is the difference between the use of high dose aspirin and low dose aspirin with regard to the risk of developing gout?

**Answer:**

The use of thiazide diuretics, cyclosporine, and low-dose aspirin (

**Tuesday, February 8, 2011****Question:**

Which antibiotics are most frequently implicated as risk factors for the development of Clostridium difficile?

**Answer:**

The cited reference points out that the antibiotics most frequently implicated prior to the year 2000 were cephalosporins, especially cefotaxime and ceftazidime, and clindamycin. More recently, fluorquinolones have emerged as major inducing agents presumably due to emergence of the NAP-1 strain. (Bartlett JG. Clostridium difficile: progress and challenges. 2010 Ann. N.Y. Acad. Sci. 1213: 6269.)

**Monday, February 7, 2011****Question:**

The geometric mean blood lead level in children aged 1-5 years declined from 14.9 micrograms per deciliter in the late 1970s to 1.9 micrograms per deciliter in 2004. What is generally regarded as the primary cause for this decline in childhood blood lead levels?

**Answer:**

Restrictions in the use of lead in paint and gasoline substantially reduced the amount of environmental lead resulting in important declines in children's blood lead levels from the 1970s to 2004. (MMWR, 60(3), January 28,2011)

**Friday, February 4, 2011****Question:**

What is Xyrem?

**Answer:**

Xyrem (sodium oxybate) is a pharmaceutical grade formulation of GHB approved for use in 2002 to treat excessive daytime sleepiness and cataplexy in patients with narcolepsy. Interestingly, this drug is shipped only directly to the patient by express carrier. If the patient is not available to sign for the shipment, the shipment is returned to the sender. When used as prescribed, Xyrem is classified as a Schedule III drug. If it is used in an illicit fashion, it is considered to be a Schedule I drug. (www.xyrem.com/healthcare-professionals/. accessed 02/02/2010)

**Thursday, February 3, 2011****Question:**

For what clinical indications is Botox currently FDA approved?

**Answer:**

Botox is currently FDA approved for the treatment of upper limb spasticity, axillary hyperhidrosis, cervical dystonia, blepharospasm, strabismus and for cosmetic reduction of wrinkles. In addition, Botox has recently been FDA approved for prevention of headache in adults with chronic migraine involving greater than or equal to 15 headache days per month for greater than or equal to 3 months.(The Medical Letter, 53(1356):7)

**Wednesday, February 2, 2011****Question:**

What is permethrin, what is the mechanism of action when used as a scabicide, and what is the basis for the selective neurotoxicity for this agent?

**Answer:**

Permethrin is a synthetic pyrethroid agent usually used topically as a 5% cream for the treatment of scabies. Permethrin interrupts voltage-gated sodium channels of arthropods resulting in prolonged depolarization of nerve-cell membranes and disruption of neurotransmission. The selective neurotoxic effect of permethrin on invertebrates is due to structural differences in voltage-gated sodium channels between vertebrates and invertebrates. (Currie BJ and McCarthy JS. Permethrin and ivermectin for scabies. 2010 N Engl J Med 362:717-725)

**Tuesday, February 1, 2011****Question:**

Anthracycline drugs such as doxorubicin are used for the treatment of a wide variety of neoplasms. The utility of these agents however is limited by dose-related cardiotoxicity manifested by arrhythmias and myocardial depression during therapy as well as cardiomyopathy that can present years after treatment. There is increasing evidence that CoQ10 administration can prevent or reduce these undesirable side effects. What is the mechanism for this potential positive effect of CoQ10?

**Answer:**

Anthracyclines-related cardiomyopathy is probably associated with irreversible oxidative damage to cardiac mitochondria. The cited reference reports these organelles contain a unique enzyme (a NADH dehydrogenase) that reduces anthracyclines to their semiquinones ultimately resulting in severe oxidative damage to mitochondrial DNA leading to apoptosis of cardiomyocytes. CoQ10 by its antioxidant action and high concentration in the inner mitochondrial membrane can reduce this oxidative damage. (Pepe S, et al. Coenzyme Q10 in cardiovascular disease. 2007 Mitochondrion 7S: S154S167)

**Monday, January 31, 2011****Question:**

The Portuguese man-of-war is recognized for the very painful stings inflicted by these organisms. What role does the application of vinegar to the injured area currently play?

**Answer:**

The cited reference points out that vinegar is no longer recommended in the management of Portuguese man-of-war stings because vinegar has been shown to initiate the firing of nematocysts. The most effective treatment for these injuries has been identified as hot water immersion for proximally 20 min. in some cases the application of local anesthetics and the use of analgesics may also become necessary. (Fernandez I, et al. encounters with venomous sea life. 2011 JEM, (1): 103112)

**Friday, January 28, 2011****Question:**

What is the fate of fentanyl that might be retained on the skin after a fentanyl patch is removed?

**Answer:**

Even after a fentanyl patch is removed, the cited reference points out that fentanyl is concentrated in the cutaneous layers beneath the site of the removed patch. Drug absorption reportedly continues into the systemic circulation from this site. Thus simple patch removal does not, in itself, cease exposure to the drug.(Moon JM and Chun BJ. Fentanyl intoxication caused by abuse of transdermal fentanyl. 2011 JEM, 40(1):37-40)

**Thursday, January 27, 2011****Question:**

What is the theory behind the notion of stone heart as it applies to the use of calcium in the face of digoxin toxicity?

**Answer:**

The cited reference explains the stone heart theory views calcium as the precipitant of an irreversible non-contractile state due to failure of diastolic relaxation resulting from calcium binding to troponin-C. (Levine M, et al. The effects of intravenous calcium in patients with digoxin toxicity. 2011 JEM, 40(1):41-46)

**Wednesday, January 26, 2011**

**Question:**

The compound 6-monoacetylmorphine (6-MAM) is a marker for exposure to what drug of abuse?

**Answer:**

6-monoacetylmorphine (6-MAM) is a marker for heroin use. Heroin is diacetylmorphine. Diacetylmorphine is rapidly hydrolyzed to 6-MAM in the early stages of heroin metabolism in humans. (Lintzeris N. Prescription of Heroin for the Management of Heroin Dependence: Current Status. 2009 CNS Drugs, 23(6):463-476)

**Tuesday, January 25, 2011**

**Question:**

Phytosterols are typical constituents of plant cell walls. These compounds have been recommended by some to provide non-prescription/ non-pharmaceutical reduction in LDL cholesterol and total cholesterol. What is the mechanism for this effect?

**Answer:**

Phytosterols compete with cholesterol molecules for incorporation into mixed micelles in the intestinal tract. A co-crystallization with cholesterol, yielding an increased fecal excretion of cholesterol, also takes place. (Marangoni F and Poli A. Phytosterols and cardiovascular health. 2010 Pharmacological Research 61:193199)

**Monday, January 24, 2011**

**Question:**

What is the current (and historical) content of benzene in gasoline?

**Answer:**

According to the cited reference, between 1972 and 1991 the average concentration of benzene in American gasoline ranged from 0.8% to 3.18%, while currently a typical American gasoline contains around one percent by volume. The historical concentration of benzene in gasoline from the European community and other countries may often be greater than two percent. A 2002 study reported that the mean benzene content of gasoline distributed in Europe ranged from one to four percent, with values reported as high as 8.6%. (Keenan JJ, et al. Gasoline: A complex chemical mixture, or a dangerous vehicle for benzene exposure? 2010 Chemico-Biological Interactions, 184: 293295)

**Friday, January 21, 2011**

**Question:**

What role do endogenous digitalis-like factors (EDLF) play in the pathophysiology of pre-eclampsia?

**Answer:**

The cited reference reports that although the precise etiology for pre-eclampsia (PE) is not known, some studies implicate placental and circulating factors in the pathophysiology of pre-eclampsia. The authors go on to indicate Among these are compounds that inhibit the sodium pump, referred to as endogenous digitalis-like factors (EDLF). They further point out Increased EDLF levels, as measured by specific antibodies to endogenous steroids (ouabain and marinobufagenin) and by cross-reacting to digoxin antibodies, have been reported in both maternal and cord blood in PE. Digoxin-binding antibody fragment has been shown to reduce blood pressure in an animal model of PE, in a postpartum trial, and in anecdotal reports in women with severe PE. The cited study reports results suggesting that digital antibodies may prevent a decline in renal function in severe (human) preeclampsia by neutralizing EDLF. Adair DC, et al. Digoxin Immune Fab Treatment for Severe Preeclampsia. 2010 American Journal of Perinatology, 27(8):665-662

**Thursday, January 20, 2011**

**Question:**

What are the EPA-designated "criteria [air] pollutants" and by what authority does EPA so designate these substances?

**Answer:**

The Clean Air Act requires EPA to set National Ambient Air Quality Standards for six common air pollutants. These commonly found air pollutants (also known as "criteria pollutants") are found all over the United States. They are particle pollution (often referred to as particulate matter), ground-level ozone, carbon monoxide, sulfur oxides, nitrogen oxides, and lead. These pollutants can harm your health and the environment, and cause property damage. Of the six pollutants, particle pollution and ground-level ozone are the most widespread health threats. EPA calls these pollutants "criteria" air pollutants because it regulates them by developing human health-based and/or environmentally-based criteria (science-based guidelines) for setting permissible levels. The set of limits based on human health is called primary standards. Another set of limits intended to prevent environmental and property damage is called secondary standards. (<http://www.epa.gov/airquality/urbanair/>)

**Wednesday, January 19, 2011**

**Question:**

What is meth mouth?

**Answer:**

The term Meth Mouth has been used to describe the widespread dental caries frequently seen in methamphetamine users. The cited reference points out that poor oral hygiene, high intake of refined carbohydrates, and increased acidity in the oral cavity from oral intake of methamphetamine, high calorie carbonated beverages, GI regurgitation or vomiting may contribute to increased number and severity of carious lesions in patients that abuse methamphetamine. (Hamamoto DT and Rhodus N. Methamphetamine abuse and dentistry. 2009 Oral Diseases 15:27-37)

**Monday, January 17, 2011**

**Question:**

What is ANTU?

**Answer:**

ANTU is alpha-naphthylthiourea and is a rodenticide that can cause liver and pulmonary injury if ingested by humans. (Sipahi EY, et al. Oxidized low density lipoproteins accumulate in rat lung after experimental lung edema induced by ANTU. 2004 Pharmacological Res. 50(6):585-591)

**Friday, January 14, 2011**

**Question:**

Wet cement (as used in the building trades) is capable of creating dermal occupational injury via three distinct mechanisms. What are they?

**Answer:**

Wet cement damages skin in three ways: 1. Allergic dermatitis as a reaction to its hexavalent chromate ions. 2. As abrasions caused by the gritty nature of the coarse and fine aggregate in the cement. 3. Wet cement has a pH of 12.5 causing alkali burns. The severity of the burn depends on the amount of abrasion created by the cement aggregate and the duration of cement contact. (Lewis PM. Wet cement remains a poorly recognized cause of full-thickness skin burns. 2004 Injury, 35:982985)

**Thursday, January 13, 2011**

**Question:**

What are the suspected causes for vancomycin- induced ototoxicity and nephrotoxicity?

**Answer:**

The cited reference indicates that vancomycin-induced ototoxicity and nephrotoxicity manifested by tinnitus/high-tone hearing loss and elevated serum creatinine levels have been correlated with persistently high vancomycin peak or trough serum levels. Today, ototoxicity is extremely unusual if serum concentrations are maintained below 30 mg/L. Renal toxicity, while uncommon, is more likely to occur when vancomycin is combined with aminoglycosides, especially in adults receiving therapy longer than 21 days and if trough vancomycin levels exceed 10 microg/mL. (Levine DP. Vancomycin: Understanding Its Past and Preserving Its Future. 2008 Southern Medical Journal, 101(3): 284-291)

**Wednesday, January 12, 2011**

**Question:**

The magico-religious (ritualistic) use of mercury among various subpopulations in the U.S. has been discussed as a potential source for environmental mercury contamination. What is the extent of mercury use for magic-religious purposes?

**Answer:**

The extent of ritualistic mercury use is unknown, but several studies have collected data that indicate its use is prevalent in some areas. In one survey of 203 Latin American and Caribbean adults in New York City; 44% of Caribbean and 27% of Latin American respondents reported mercury use. Six percent of Latin American and 12% of Caribbean mercury users said they used it daily; 54% of Latin American and 50% of Caribbean mercury users said they used it occasionally. Eighty-two percent said they obtained elemental mercury from a botanica; 3% brought it with them when they emigrated to the United States; 6% got it from their job, a pharmacy, their landlord, or their parents; and 9% did not specify a source. (Task Force on Ritualistic Uses of Mercury Report. December 2002. <http://www.epa.gov/superfund/community/pdfs/mercury.pdf>)

**Tuesday, January 11, 2011****Question:**

*Clostridium tetani* is a gram-positive, spore-forming, obligate anaerobic bacillus. It is a common soil bacterium whose spores are ubiquitous in nature. These spores can be found in the soil as well as in the intestines and feces of domestic animals and humans. Tetanus is caused by two toxins secreted by *C. tetani*. What are these toxins and what is their respective mechanisms of action?

**Answer:**

The cited reference indicates the primary toxin is a neurotoxin known as tetanospasmin. Tetanospasmin is responsible for the characteristic muscle spasms associated with tetanus. However, the role of the second toxin, tetanolysin, is still not well understood. Tetanospasmin prevents the release of gamma-aminobutyric acid (GABA) at the junction of inhibitory nerve synapses. Lack of GABA prevents inhibition of sustained excitatory nervous impulses, causing the clinical signs of tetanus. (Rhee P, et al. Tetanus and Trauma: a review and recommendations. 2005 J Trauma, 58:1082-1088)

**Monday, January 10, 2011****Question:**

Metoclopramide is a dopamine receptor antagonist used for treatment of a variety of gastrointestinal symptoms during the past three decades. In 2009, the FDA issued a black box warning regarding long-term or high-dose use of this medication because of the risk of developing tardive dyskinesia (TD). What is the actual risk for TD associated with the use of metoclopramide?

**Answer:**

The cited reference indicates that the risk of tardive dyskinesia from metoclopramide use is likely to be less than 1%, much less than the estimated 110% risk previously suggested in national guidelines. (Rao AS and Camilleri M. Review article: metoclopramide and tardive dyskinesia. 2009 Alimentary Pharmacology & Therapeutics 31(1):11-19)

**Friday, January 7, 2011****Question:**

What are the hypothesized causes of sudden death in individuals who have recently used MDMA?

**Answer:**

The cited reference points out that little is known about the etiology of sudden death in individuals who had taken MDMA. However, it seems likely that the sympathomimetic effects of the drug may precipitate a dysrhythmic catastrophe. This may occur in an otherwise perfectly healthy individual. However, undiagnosed cardiomyopathy, hypertension or viral myocarditis may be involved. A number of other congenital cardiac conduction abnormalities may go undiagnosed in young people (such as Wolff-Parkinson-White, Romano-Ward, Brugada, and Jervell and Lange-Nielsen Syndromes). These individuals are probably at risk of sudden death from excessive sympathetic stimulation. Furthermore, a long QT interval has been reported in association with MDMA toxicity. (Hall AP and Henry JA. Acute toxic effects of Ecstasy (MDMA) and related compounds: overview of pathophysiology and clinical management. 2006 Br J Anaesth 96 (6): 678-685)

**Thursday, January 6, 2011****Question:**

A massive outbreak of waterborne illness occurred in the greater Milwaukee area during late March and early April of 1993. What was the infectious agent involved in this outbreak and how many people were estimated to have been affected?

**Answer:**

The outbreak in question involved waterborne cryptosporidium infection and it has been estimated that more than 400,000 people were affected. (MacKenzie WR, et al. A massive outbreak in Milwaukee of cryptosporidium infection transmitted through the public water supply. 1994 NEJM 331(3):161-167)

**Wednesday, January 5, 2011****Question:**

Opsoclonus is an ocular movement disorder described as "involuntary, irregular, back-to-back, multivectorial, saccadic eye movements while the gaze is fixed". Opsoclonus has been described after viral infection and paraneoplastic encephalitis as well as following the ingestion of a variety of drugs. What drugs have been associated with the development of this ocular movement disorder?

**Answer:**

Opsoclonus has been described following the ingestion of organophosphates, lithium, cetirizine, amitriptyline, and diphenhydramine, among other substances. (Shaun D, et al. Opsoclonus Due to Diphenhydramine Poisoning. 2010 N Engl J Med; 363:e40 December 30, 2010)

**Tuesday, January 4, 2011****Question:**

What is the mechanism of action for the rodenticide norbormide?

**Answer:**

Norbormide (NRB) is a vasoactive compound introduced to the market as a rodenticide approximately 30 years ago. NRB is uniquely toxic to rats and relatively harmless to other rodents and mammals. According to the cited reference, NRB displays unique species-specific constrictor activity that is restricted to the peripheral arteries of the rat. In arteries from all other species tested, as well as in rat aorta and extravascular smooth muscle tissue, NRB exhibits vasorelaxant properties at concentrations that induce vasoconstriction in the rat peripheral arteries. (Rennison D., et al. Synthesis and activity studies of analogues of the rat selective toxicant norbormide. 2007 Bioorganic & Medicinal Chem 15:2963-2974)

**Monday, January 3, 2011****Question:**

What is kohl?

**Answer:**

Also known as surma, kohl is often used as eyeliner cosmetic in the Middle East, Asia and Africa. Traditionally, fine kohl powder is applied to the conjunctive surface of the eyelids in the same way that mascara is applied to the outer surface. The use of kohl for medical and cosmetic purposes can be traced back over many centuries. It has been used to stop bleeding and after circumcision. The cited study of kohl samples demonstrated high levels of lead, aluminum, and antimony. Some samples were also found to contain camphor and menthol. Blood sampled from regular kohl users revealed elevated blood lead levels and relatively low hemoglobin levels. (Al-Ashban RM, et al. Kohl (surma): a toxic traditional eye cosmetic study in Saudi Arabia. 2004 Public Health, 118: 292298)

**Friday, December 31, 2010****Question:**

What are trichothecenes?

**Answer:**

The cited reference indicates that trichothecenes are low molecular weight compounds that are potent inhibitors of protein synthesis, with secondary effects on DNA and RNA synthesis. Rapidly dividing cells are the most susceptible to trichothecenes, and are often referred to as radiomimetic agents, as they mimic the signs and symptoms of radiation sickness. Although the mechanisms of action of these toxins are not completely known, they probably act by interfering with peptidyl transferase activity during mRNA translation. This effectively inhibits protein production. (Henghold WB. Other biologic toxin bioweapons: ricin, staphylococcal enterotoxin B, and trichothecene mycotoxins. 2004 Dermatol Clin 22:257262)

**Thursday, December 30, 2010****Question:**

What is betel quid and what medical problems have been reported in association with the use of this material?



**Answer:**

Betel quid is a material that usually contains areca nut (*Areca catechu*), lime and catechu wrapped in a betel leaf. Tobacco is often added. Betel quid is used for its mild stimulant and purported medicinal properties. It is usually chewed in combination with Piper betle (inflorescence or leaf) and lime and is used by approximately 10% of the world population. Betel quid use is associated with an increase in the risk for oral cancer, liver cirrhosis, and hepatocellular carcinoma. In addition betel-quid use is associated with obesity, hypertension, diabetes, hyperlipidemia, and the metabolic syndrome. (Guh JY, et al. Betel quid use associated with heart disease in women. 2007 Am J Clin Nutr, 85:1229-35.

**Wednesday, December 29, 2010****Question:**

What is HU-210?

**Answer:**

HU-210 is a synthetic cannabinoid mimicking compound, [(6aR,10aR)-9-(hydroxymethyl)-6,6-dimethyl-3-(2-methyloctan-2-yl)-6a,7,10,10a-tetrahydrobenzo[c] chromen-1-ol]. It has been identified in a variety of synthetic cannabinoid mimicking substances for sale on the Internet and elsewhere including: Spice Gold, Spice Silver, Spice Diamond, Genie, and Yucatan Fire. In addition to HU-210, there are at least half a dozen other compounds with similar structures, plus several unrelated compounds that have cannabinoid mimicking effects (notably JWH-018 (1-pentyl-3-(1-naphthoyl)indole)), that are being used to adulterate the plant materials in Spice and similar products. Some reports indicate that HU-210 may be hundreds of times more potent than THC; thus, even with trace amounts detected in the materials being sold, these materials may be viewed as stealth marijuana. (Microgram Bulletin, March, 2009, 42(3): 23-24, US Dept of Justice, Drug Enforcement Administration and Anthony J. Scalzo, MD personal communication, December, 2010)

**Tuesday, December 28, 2010****Question:**

The chemical titanium dioxide (TiO<sub>2</sub>) is manufactured worldwide in substantial quantities. What is the primary industrial use for this chemical?

**Answer:**

Titanium dioxide is most commonly used to impart a white/bright color to paints, coatings, papers and plastic products. Titanium dioxide containing pigments are also used in many foods, pharmaceuticals, ceramics, fibers, and rubber products. (Hext PM, et al. Titanium dioxide: Inhalation toxicology and epidemiology. 2005 Ann Occup Hyg. 49(6):461-472)

**Monday, December 27, 2010****Question:**

The use of cocaine more than two times per week for longer than six months has been reported to lead to a variety of serious gastrointestinal problems; what are they?

**Answer:**

The use of cocaine more than two times per week for longer than six months has been reported to lead to mesenteric thrombosis, perforation, and visceral ischemia in the lower gastrointestinal tract. (Ellis CN and McAlexander WW. Enterocolitis Associated With Cocaine Use. 2005 Dis Colon Rectum, 48: 2313-2316)

**Friday, December 24, 2010****Question:**

Mistletoe extracts are sometimes used to treat cancer patients in concert with claims that mistletoe extract improves quality of life as well as survival. Is mistletoe extract, in fact, efficacious in this regard?

**Answer:**

A recent Cochrane Database of Systematic reviews concluded: "The evidence from RCTs to support the view that the application of mistletoe extracts has impact on survival or leads to an improved ability to fight cancer or to withstand anticancer treatments is weak. Nevertheless, there is some evidence that mistletoe extracts may offer benefits on measures of QOL during chemotherapy for breast cancer, but these results need replication. Overall, more high quality, independent clinical research is needed to truly assess the safety and effectiveness of mistletoe extracts". Horneber MA, et al. Mistletoe therapy in oncology. 2008 Cochrane Database of Systematic Reviews. (2):CD003297.)

**Thursday, December 23, 2010****Question:**

Nutmegs, the seeds of the evergreen tropical tree *Myristica fragrans* Houtt., are mainly used as a spice. They are described to be psychoactive when ingested in high doses. What are the main chemical constituents of nutmeg?

**Answer:**

The primary constituents of the volatile oil of nutmeg are the alkenebenzene derivatives elemicin (1-(30,40,50-trimethoxyphenyl)-prop-2-ene; EL), myristicin (1-(30,40-methylenedioxy-50-methoxyphenyl)-prop-2-ene; MY), and saffrole (1-(30,40-methylenedioxyphenyl)-prop-2-ene; SA). (Beyer J, et al. Abuse of Nutmeg (*Myristica fragrans* Houtt.): Studies on the metabolism and the toxicologic detection of its ingredients elemicin, myristicin, and saffrole in rat and human urine using gas chromatography/ mass spectrometry. 2006 Ther Drug Monitoring, 28:568-575)

**Wednesday, December 22, 2010****Question:**

Methyl bromide is a colorless, halogenated, aliphatic, hydrocarbon that has been used as a fumigant, as a fire retardant and as a refrigerant. Occupational exposure to this chemical may occur via the inhalation and/or dermal routes. What are the acute clinical problems associated with methyl bromide toxicity?

**Answer:**

Acute methyl bromide toxicity usually involves central nervous system problems that may include dizziness, nausea, vomiting, ataxia, and myoclonus of the tongue, face and all limbs. While a number of theories have been advanced, it is important to recognize that the mechanisms of methyl bromide toxicity have not yet been fully elucidated. (Hoizey G, et al. An unusual case of methyl bromide poisoning. 2002 Clin Tox 40(6):817-821)

**Tuesday, December 21, 2010****Question:**

Priapism is defined as a painful, prolonged and sustained erection occurring in the absence of sexual stimulation. What drugs and toxins have been reported to cause priapism?

**Answer:**

A wide variety of drugs and toxins have been reported to cause priapism including; chlorpromazine, thioridazine, fluphenazine, perphenazine, mesoridazine, thiothixine, haloperidol; zuclopenthixol, clozapine, risperidone, olanzapine, aripiprazole, quetiapine, Terazosin, tamsulosin, alfuzosin, prazosin, hydralazine, trazodone, nefazadone, fluoxetine, bupropion, citalopram, sertraline, buspirone, hydroxyzine, ethanol, cocaine, ecstasy, marijuana, tadalafil, sildenafil, vancomycin, testosterone, gonadotropin releasing hormone, propofol, scorpion sting, and black widow spider. (Sood S., et al Priapism associated with atypical antipsychotic medications: a review. 2008 International Clinical Psychopharmacology 23 (1):9-17)

**Monday, December 20, 2010****Question:**

What are the clinical characteristics of wound botulism?

**Answer:**

Wound botulism is characterized by bilateral cranial neuropathies in conjunction with descending symmetric muscle weakness. (Sam AH and Beynon HLC. Wound botulism. 2010 NEJM 363(25):25)

**Friday, December 17, 2010****Question:**

What is welders siderosis?

**Answer:**

Welders siderosis refers to the pneumoconiosis caused by inhalation of iron oxide particles produced in the welding process and is generally considered to be a benign form of lung disease. (Patel RR, et al. Systemic iron overload associated with welders siderosis. 2009 Am J Med Sciences 337(1):57-59.

**Thursday, December 16, 2010****Question:**

In some rare cases, digoxin toxicity has been reported to be associated with visual disturbances. What are these visual disturbances?



**Answer:**

The visual disturbances reported to be associated with digoxin toxicity include flashing lights, halos, and color disturbances involving yellow-green patterns. However, the most commonly reported visual problem is hazy or blurred vision. (Bauman JL, et al. Mechanisms, manifestation and management of digoxin toxicity in the modern era. 2006 Am J Cardiovasc Drugs 6(2):77-86)

**Wednesday, December 15, 2010****Question:**

How many people were injured as a result of the sarin nerve agent attack in Tokyo, Japan, on March 20, 1995?

**Answer:**

According to the cited reference, more than 5,500 civilians, including members of the rescue teams, were injured. Most of them (4,073) suffered only mild symptoms (mainly ocular) and were discharged from hospital after a few hours; 984 victims suffered moderate injuries, without the need for mechanical ventilation, 50 victims had severe injuries and needed mechanical ventilation and resuscitation, and 12 people died as a result of the attack. (Hoffman A, et al. A decade after the Tokyo sarin attack: A review of neurological follow-up of the victims. 2007 Military Medicine, 172(6):607-611)

**Tuesday, December 14, 2010****Question:**

The most likely routes for human exposure to uranium involves inhalation and/or ingestion. What is the expected toxicity of uranium with regard to the following organ systems in humans: cardiovascular, musculoskeletal, endocrine, GI, and skin? What are the effects of uranium exposure on human reproduction?

**Answer:**

No significant toxicity of uranium has been evidenced with regard to the cardiovascular, musculoskeletal, endocrine, GI, and dermal organ systems. No effects on reproduction have been reported in humans from uranium exposure. (Vicente-Vicente L, et al. of uranium: Nephrotoxicity, pathophysiological, diagnostic and therapeutic perspectives. 2010 Toxicological Sciences 118(2):324-347)

**Monday, December 13, 2010****Question:**

The inhalation of one form of chromium has been associated with the development of one form of cancer. What is this form of chromium and what is the cancer that has been associated with it?

**Answer:**

The inhalation of hexavalent (VI) chromium has been associated with the development of pulmonary cancer in some individuals. (Smith AH and Steinmaus CM. Health Effects of Arsenic and Chromium in Drinking Water: Recent Human Findings. 2009 Annu. Rev. Public Health, 30:10722)

**Friday, December 10, 2010****Question:**

In utero exposure to methadone may, in some cases, induce a well-described neonatal abstinence syndrome (NAS). What are the clinical characteristics of this NAS?

**Answer:**

The NAS induced by in utero methadone exposure is characterized by central nervous system hyperirritability and autonomic nervous system dysfunction as well as gastrointestinal tract and respiratory system dysfunction. Untreated NAS can result in serious illness including diarrhea, feeding difficulties, weight loss, seizures and death. In most cases, methadone-associated NAS requires prolonged hospitalization, pharmacologic intervention, and continuous monitoring. (Jones HE, et al. Neonatal abstinence syndrome after methadone or buprenorphine exposure. 2010 NEJM 363(24): 2320-2331)

**Thursday, December 9, 2010****Question:**

Ingestion of the seeds of the plant Thevetia peruviana (yellow oleander) result in large numbers of annual poisonings in South Asia where the resulting rate of morbidity and mortality is high. Yellow oleander seeds contain potentially harmful cardiac glycosides. What are these potentially harmful cardiac glycosides?

**Answer:**

The potentially harmful cardiac glycosides contained in the seeds of Thevetia peruviana include thevetins A and B and neritofolin. These seeds may also contain other, yet to be unidentified, harmful glycosides. (Rajapakse S. Management of yellow oleander poisoning. 2009 Clinical Toxicology 47:206212)

**Wednesday, December 8, 2010****Question:**

A non-traditional testing matrix has been used to track the epidemiology of lead exposure in children in the Cleveland area during the latter two thirds of the 20th century. What was that matrix and why was that chosen as a study vehicle instead of the more common blood lead measurements?

**Answer:**

The cited reference notes Childhood uptake of lead from exposure to atmospheric leaded gasoline in the United States has been studied using mainly blood lead levels. Since reliable blood lead techniques were used only after the peak use of leaded gasoline, the prior exposure history is unclear. The well-documented decline in blood lead levels after the mid-1970s could represent the continuation of a historic steady decline in exposure from many sources. Alternatively, the post-1970s decline might represent the declining phase of a unimodal rise and fall corresponding closely to usage of leaded gasoline. To assess these possibilities, lead concentration and 207Pb/206Pb isotope ratios were measured in the enamel of permanent molar teeth formed between 1936 and 1993 in mainly African-American donors who grew up in the Cleveland area. Tooth enamel preserves the lead concentration and isotope ratio that prevails during tooth formation. (Robbins N, et al. Childhood lead exposure and uptake in teeth in the Cleveland area during the era of leaded gasoline. 2010 Science of the Total Environment 408: 41184127)

**Tuesday, December 7, 2010****Question:**

More than 500 species of marine snails (cone shells) are thought to be venomous with fewer than two dozen species reported to cause human envenomations. What are the characteristics of cone shell envenomation in humans?

**Answer:**

Victims of cone shell envenomation typically first perceive a local stinging sensation that rapidly evolves into intense local pain. Localized paresthesias develop and may rapidly become generalized. Paresthesias often are followed by bulbar and generalized areflexic weakness. Victims may also develop respiratory insufficiency, coma, disseminated intravascular coagulation, heart failure and rapid death. The cited reference points out that species with shells displaying prominent geometric designs of bright colors are more likely to attract the human shell collector, and tapping on the shell or placing the cone snail in a pocket are common risks for envenomation. (Watters MR. Tropical marine neurotoxins: Venoms to drugs. 2005 Seminars in Neurology, 25(3):278-289)

**Monday, December 6, 2010****Question:**

What are the risk factors that have been identified with an increased mortality associated with valproate toxicity?

**Answer:**

The risk factors that have been identified with an increased mortality associated with valproate toxicity include patients less than 2 years of age, those with developmental delay and co-existing metabolic disease. The cited reference notes that the patients at greatest risk are those with complex neurological disorders requiring multiple anti-seizure medications. (Katiyar A and Aaron C. Case files of the Childrens Hospital of Michigan Regional Poison Center: The use of carnitine for the management of acute valproic acid toxicity. 2007 J Med Tox, 3(3):129-138)

**Friday, December 3, 2010****Question:**

Following metformin overdose which patients are most likely to die?

**Answer:**

The cited study concluded that patients with metformin overdose with more profound acidemia and greater increases in their serum lactate and metformin concentrations were more likely to die than those with less significant laboratory derangements. (Dell'Aglio, DM et al. Acute Metformin Overdose: Examining Serum pH, Lactate Level, and Metformin Concentrations in Survivors Versus Nonsurvivors: A Systematic Review of the Literature. 2009, Anns Emerg Med) 54 (6): 818-823)

**Thursday, December 2, 2010****Question:**

What is tardive dyskinesia and historically what drug was first implicated in the development of tardive dyskinesia?

**Answer:**

Tardive dyskinesia results from chronic exposure to dopamine receptor blocking agents and refers to a syndrome that presents with rapid, repetitive, stereotypic movement involving the oral, buccal, and lingual areas. Tardive dyskinesia was first described within five years following the introduction of the first dopamine receptor blocking agent, chlorpromazine in the 1950s. (Soares-Weiser K and Fernandez H. Tardive dyskinesia. 2007 Seminars in Neurology, 27 (2): 159-169)

**Wednesday, December 1, 2010****Question:**

Studies in the 1960s and 1970s reported that repeated administration of tetracyclines to young children resulted in discoloration of developing teeth. More recent studies have indicated that doxycycline, specifically, is associated with no or only negligible staining of teeth. To what is this difference in teeth staining between doxycycline and other tetracyclines attributed?

**Answer:**

The difference is generally attributed to the lower binding affinity of doxycycline for calcium. (Volovitz B et al. Absence of tooth staining with doxycycline treatment in young children. 2007 Clin Pediatrics 46(2):121-126)

**Tuesday, November 30, 2010****Question:**

What is the optimal treatment for sea urchin envenomation?

**Answer:**

The optimal treatment for sea urchin envenomation is unclear and published recommendations vary widely. Most agree that standard wound care, analgesics, and warm water immersion are reasonable acute treatment options. Some recommend that any embedded urchin spines be removed but this is made difficult by their brittle nature and the fact that extensive soft tissue exploration could cause more harm than good. Most agree, however, that urchin spines that penetrate a joint space or any vital structure should be removed if at all possible. (Morocco A. Sea urchin envenomation. 2005 Clin Tox 43:119-120)

**Monday, November 29, 2010****Question:**

Spina bifida is among the most common and serious congenital malformation of humans. Although spina bifida is compatible with life, 99% of affected persons are handicapped. The prevalence of spina bifida varies from 0.2 to 3 per 1,000 total births by region, period, race and ethnicity. Both environmental and hereditary factors may contribute to the induction of spina bifida. Paternal exposure to what chemical has been linked to the development of spina bifida?

**Answer:**

A recent systematic review revealed the overall relative risk (RR) for spina bifida associated with paternal exposure to Agent Orange was 2.02 (95% confidence interval [CI]: 1.482-74), with no statistical evidence of heterogeneity across studies. (Ngo AD. Paternal exposure to Agent Orange and spina bifida: a meta-analysis. 2010 Eur J Epidemiol, 25:3744)

**Friday, November 26, 2010****Question:**

Symptoms of gastroesophageal reflux are common in pregnancy and these symptoms are often treated using proton-pump inhibitors (PPIs) in early pregnancy. What is the incidence of birth defects associated with the use of PPIs in early pregnancy?

**Answer:**

In a recently reported large cohort (more than 800,000 live births with more than 5000 exposures to PPIs) exposure to PPIs during the first trimester of pregnancy was not associated with a significantly increased risk of major birth defects. (Pasternak B., et al. Use of Proton-Pump Inhibitors in Early Pregnancy and the Risk of Birth Defects. 2010 NEJM, 363:2114-2123)

**Thursday, November 25, 2010****Question:**

4,4'-Diaminodiphenylsulphone (Dapsone) is widely used for a variety of infectious, immune and hypersensitivity disorders, with indications ranging from Hansen's disease, inflammatory disease and insect bites. Complications reported to be associated with dapsone include methemoglobinemia, bone marrow aplasia, hemolytic anemia, peripheral neuropathy and the potentially fatal dapsone hypersensitivity syndrome (DHS). What are the clinical manifestations of DHS?

**Answer:**

DHS typically presents with a triad of fever, skin eruption, and internal organ (lung, liver, neurological and other systems) involvement, occurring several weeks to as late as 6 months after the initial administration of the dapsone. (Kosseifi SG. The Dapsone Hypersensitivity Syndrome revisited: a potentially fatal multisystem disorder with prominent hepatopulmonary manifestations. 2006 Journal of Occupational Medicine and Toxicology, 1:1-9)

**Wednesday, November 24, 2010****Question:**

Methacholine challenge testing is one method of assessing airway responsiveness. Airway hyperresponsiveness is one of the features that may contribute to a diagnosis of asthma. Is methacholine challenge testing more useful in excluding the diagnosis of asthma or in establishing the diagnosis of asthma?

**Answer:**

Methacholine challenge testing is more useful in excluding a diagnosis of asthma than in establishing one because its negative predictive power is greater than its positive predictive power. (American Thoracic Society. Guidelines for Methacholine and Exercise Challenge Testing-1999. 2000 Am J Respir Crit Care Med (161):309-329)

**Tuesday, November 23, 2010****Question:**

What decrements in functional ability have been identified with regard to marijuana use and driving ability?

**Answer:**

In driving studies, the strongest decrements were in the drivers abilities to concentrate and maintain attention, estimate time and distance, and demonstrate coordination on divided attention tasks, all important requirements for driving. (Huestis,MA. Estimating the Time of Last Cannabis Use from Plasma 9-Tetrahydrocannabinol and 11-nor-9-Carboxy-9-Tetrahydrocannabinol Concentrations. 2005 Clin Chem 51(12): 2289-2295)

**Monday, November 22, 2010****Question:**

n-Hexane is a solvent widely used in the manufacture of adhesives, lacquers, dyes and paints. Toxicological studies have shown that it can cause a polyneuropathy classically described by Spencer and Schaumburg in 1976. How is this particular polyneuropathy characterized and what metabolite of n-hexane is responsible for these effects?

**Answer:**

The polyneuropathy associated with n-hexane is a distal central-peripheral axonopathy. The primary metabolite of n-hexane is 2,5-hexanedione (2,5-HD). 2,5-HD has been shown to be responsible for the polyneuropathy associated with n-hexane. (Prieto MJ et al. Free and total 2,5-hexanedione in biological monitoring of workers exposed to n-hexane in the shoe industry. 2003 Toxicology Letters 145: 249260)

**Friday, November 19, 2010****Question:**

Ingestion of what plant has been associated with "purple vision"?

**Answer:**

Aconitum napellus, also called monkshood or wolfsbane is a potentially hazardous plant growing in mountainous regions of Europe, Asia, and North America. One published report has documented a dyschromatopsia consisting of "purple vision" following the ingestion of Aconitum napellus. (Bonnici K, et al. Flowers of evil. 2010 The Lancet 376(9752):1616) and Moritz F, et al. Severe Acute Poisoning with Homemade Aconitum napellus Capsules: Toxicokinetic and Clinical Data. 2005 Clin Tox 43:873876)

**Thursday, November 18, 2010****Question:**

What are the hemodynamic effects often seen following the ingestion of a large single dose of thallium?

**Answer:**

Following a large single dose of thallium, there is often initial hypotension and bradycardia owing to direct effects of the sinus node and cardiac muscle, followed by hypertension and tachycardia thought to be due to vagal nerve degeneration. (Peter AL and Viraraghavan T. Thallium: a review of public health and environmental concerns. 2005 Env International 31:493-501)

**Wednesday, November 17, 2010****Question:**

What is the association between aspirin intolerance and nasal polyps?

**Answer:**

In 70% of ASA-intolerant patients, nasal polyps can be found; whereas in the general population the overall prevalence of nasal polyps is only about 4%. Typical for the polyps in ASA-intolerant patients is their aggressive growth that involves all paranasal sinuses bilaterally. The pathogenesis of aspirin intolerance is not an IgE-mediated reaction, but is related to an abnormal metabolism of arachidonic acid implicating both the lipoxygenase (LO) and the cyclooxygenase (COX) pathways. (Klimek L and Pfaar O. Aspirin Intolerance: Does Desensitization Alter the Course of the Disease? 2009 Immunol Allergy Clin N Am (29): 669675)

**Tuesday, November 16, 2010****Question:**

Physostigmine is a short-acting acetylcholinesterase inhibitor that slows the degradation of acetylcholine in the synapse. This results in an increase in acetylcholine concentrations and thus helps overcome postsynaptic blockade caused by anticholinergic agents. How does physostigmine differ from other cholinesterase inhibitors such as neostigmine and pyridostigmine?

**Answer:**

Unlike neostigmine and pyridostigmine, physostigmine has a tertiary amine structure that allows it to pass freely into the central nervous system causing reversal of both central and peripheral anticholinergic symptoms. (Frasconga N. Physostigmine: is there a role for this antidote in pediatric poisonings? 2007 Current Opinion in Pediatrics, 19:201205)

**Monday, November 15, 2010****Question:**

Who was the first female Professor at Harvard University also known as the "founder" of American occupational toxicology.

**Answer:**

Dr. Alice Hamilton was the pioneer physician who first began to develop the current paradigms of industrial hygiene and occupational toxicology in American Industry. Her book entitled "Exploring the Dangerous Trades" should be required reading for all those with an interest in the history of medical and occupational toxicology. (Baron SL and Brown TM. Alice Hamilton (1869-1970): Mother of US Occupational Medicine. 2009 Am J Pub Health Supple 3; 99(S3):S548.

**Thursday, November 11, 2010****Question:**

Bowen's Disease is a premalignant condition also known as intradermal carcinoma in situ. This disorder has been noted as a complication in a chronic exposure to a specific toxicant. Name the toxicant.

**Answer:**

Bowen's Disease has been noted as a complication of chronic arsenicosis. (Mukherjee SC, et al. Murshidabad- One of the nine groundwater arsenic affected districts of West Bengal, India, part II: dermatological, neurological and obstetric findings. 2005 Clin Tox 43(7):835-848)

**Wednesday, November 10, 2010****Question:**

The consumption of coffee and tea has been theorized to have beneficial effects with regard to the development of stroke in some patients. What is the proposed mechanism for this potentially beneficial effect?

**Answer:**

Coffee consumption could plausibly influence the risk of cardiovascular disease because coffee has antioxidant properties and may improve insulin sensitivity. (Larsson S., et al. Coffee and tea consumption and risk of stroke subtypes in male smokers. 2008 Stroke 39(6):1681-1687

**Tuesday, November 9, 2010****Question:**

Black cohosh, rhizomes of Cimicifuga racemosa or Actaea racemosa, has been used traditionally for a variety of female complaints which include pain during childbirth, uterine colic, and dysmenorrhea. This herbal preparation contains triterpene glycosides (acetin, 23-epi-26- deoxyactein [formerly called 27-deoxy- actein], cimicifugoside), phenolic acids (isoferulic acid, fukinolic acid), flavonoids, volatile oils, tannins, and other pharmaco- logically active ingredients. What safety concerns have been raised concerning the use of black cohosh?

**Answer:**

A variety of preclinical and clinical studies suggest black cohosh to be relatively safe; however, many of these studies have been of short duration and some poorly designed. Several safety concerns about black cohosh include hepatotoxicity, herb-drug interaction, cardiovascular disease multiorgan failure, anaphylactic facio-oral edema, and cutaneous vasculitis. (Borrelli F and Ernst E. Black cohosh (Cimicifuga racemosa): a systematic review of adverse events. 2008 Am J Ob Gyn 199(5):455-466)

**Monday, November 8, 2010****Question:**

What is "PEG"? What do the numbers often appended to the term "PEG" mean and how does that number relate to potential toxicity for these molecules?

**Answer:**

PEG is polyethylene glycol, a polymer made up of identical ethylene glycol subunits. PEG's have a descriptor associated with them that represents the mean molecular weight of the molecule. So PEG 200 has a molecular weight of 200; PEG 400 has a molecular weight of 400, etc, etc. Generally the toxicity of larger molecular weight PEG molecules is less than that of lower molecular weight molecules. (Webster R, et al. PEGylated proteins: Evaluation of their safety in the absence of definitive metabolic studies. 2007 Drug Met Disposition 35:9-16)

**Friday, November 5, 2010****Question:**

The only formulation of quinine sulfate currently available in the US is the drug Quaaliquin. This drug is FDA approved for the treatment of uncomplicated malaria only however the drug is usually used for the treatment of nocturnal leg cramps. The FDA recently issued a safety warning for this drug. What is the issue that prompted the issuance of this warning?

**Answer:**

38 cases of serious adverse effects of quinine have been reported to FDA recently. These generally involved thrombocytopenia that developed at about day 13 following initiation of quinine therapy. The thrombocytopenia usually reverses on stopping the drug. The cited reference points out that quinine can also cause a syndrome of tinnitus, headache, visual disturbances and nausea (cinchonism) as well as QT prolongation. (The Medical Letter, Nov 1, 2010, 52(1350):88)

**Thursday, November 4, 2010****Question:**

What is an IDLH?

**Answer:**

IDLH stands for "Immediately Dangerous to Life or Health" and generally refers to chemical inhalation hazards. The IDLH level is most often reported in parts per millions or mg/m<sup>3</sup>. IDLH's are promulgated by NIOSH and other organizations. One of the considerations for an IDLH value is: "The ability to escape without loss of life or immediate or delayed irreversible health effects. (Thirty minutes is considered the maximum time for escape so as to provide some margin of safety in calculating an IDLH value.)" (<http://www.cdc.gov/niosh/idlh/idlh-1.html>)

**Wednesday, November 3, 2010****Question:**

What are so called "chrome holes"?

**Answer:**

Chromic acid and its compounds are industrial chemicals that historically have been known to produce ulceration and perforation of the nasal septum. The first report on the subject was presented more than a century ago. Early reports about "chrome holes" involved bichromate workers with ulcerative lesions chiefly situated on the skin of the hands and arms as well as the septum of the nose. (Lieberman H. Chrome ulcerations of the nose and throat. 1941 NEJM 225(4):132-133)

**Tuesday, November 2, 2010****Question:**

The ingestion of some mushrooms containing the chemical orellanine can result in serious disease. What organ system can be affected following ingestion of these mushrooms?

**Answer:**

The ingestion of orellanine-containing mushrooms have been reported to induce acute and/or chronic renal failure. (Judge BS, et al. Ingestion of a newly described North American mushroom species from Michigan resulting in chronic renal failure: Cortinarius orellanosus. 2010 Clin Tox 48(6):545-549)

**Monday, November 1, 2010****Question:**

The ingestion of concentrated hydrogen peroxide has been associated with a variety of serious clinical problems. What are these problems?

**Answer:**

Venous and arterial gas embolism, hemorrhagic gastritis, GI bleeding, shock and death are the serious problems that may result from the ingestion of concentrated hydrogen peroxide. (French LK, et al Hydrogen peroxide ingestion associated with portal venous gas and treatment with hyperbaric oxygen: a case series and review of the literature. 2010 Clin Tox 48(6):533-538)

**Thursday, October 28, 2010****Question:**

Vitreous humor (VH) is a specimen routinely collected during autopsy in medicolegal death investigations. The use of VH for the analysis of electrolytes, glucose and nitrogen compounds as well as some drugs of abuse is well established. VH is not an acceptable matrix to determine the presence of which drug of abuse?

**Answer:**

The fact that marijuana cannabinoids are highly lipid soluble and the vitreous humor is primarily composed of water makes it virtually impossible to identify cannabinoids in the vitreous humor. (Jenkins AJ and Oblock J. Phencyclidine and cannabinoids in vitreous humor. 2008 Legal Med 10:201-203)

**Wednesday, October 27, 2010****Question:**

In the past, outbreaks of so-called "beer drinkers cardiomyopathy" have been reported. What toxicant has been implicated in this syndrome and what are the clinical manifestations associated with this problem?

**Answer:**

This syndrome has been reported in individuals consuming large quantities of cobalt fortified beer. This syndrome is characterized by pericardial effusion, elevated hemoglobin concentrations, and congestive heart failure. (Barceloux D. Cobalt. 1999 J Tox Clin Tox. 37(2):201-206)

**Tuesday, October 26, 2010****Question:**

What is the time of onset of effects, time of peak effects, and duration of effects of the substance MDMA?

**Answer:**

The onset for effects of MDMA is usually 20-60 minutes and the peak time of effect is 60-90 minutes after ingestion. The duration of effects of this substance ranges from 3 to 5 hours. (Green AR. The pharmacology and clinical pharmacology of 3,4-methylenedioxymethamphetamine (MDMA, Ecstasy) 2003 Pharm Rev 55(3):463-508)

**Monday, October 25, 2010****Question:**

What is (was) Epping jaundice?

**Answer:**

An outbreak of jaundice occurred in the Epping district of Essex, England, in February 1965. 84 persons were affected in this event wherein liver biopsies showed cholestasis. All those affected had eaten wholemeal bread made at an Epping bakery. A sack of flour from which the wholemeal bread was made had been delivered to the bakery in the same van as that used on the same day for transporting a plastic jar containing 4,4'-diaminodiphenylmethane (an aromatic amine, dissolved in butyrolactone) that was found to have been spilt in the van. This chemical was identified as the cause for Epping jaundice. (Kopelman H, et al. The Epping jaundice. 1966 Br Med J 1:514-516.)

**Friday, October 22, 2010****Question:**

What is the so-called "grey baby syndrome" and what are the clinical characteristics of this syndrome?

**Answer:**

The grey baby syndrome was first reported in 1959 in association with the use of the antibiotic chloramphenicol in infants. These babies developed abdominal distension, vomiting, cyanosis, cardiovascular collapse, irregular respirations and subsequent death shortly after initiation of therapy with chloramphenicol. Pharmacokinetic studies in neonates showed accumulation of chloramphenicol in plasma due to impaired drug metabolism. A reduction in the total daily dosage from 100 to 50 mg/kg prevented the development of the grey baby syndrome. (McIntyre J and Choonara I. Drug toxicity in the neonate. 2004 Biol of the Neonate 86:218-221)

**Thursday, October 21, 2010****Question:**

What is mechanism for the production of phocomelia (limb defects) associated with the drug thalidomide?

**Answer:**

The cited article points out that the drug thalidomide itself is not teratogenic. The monocarboxylic and dicarboxylic acid metabolites of thalidomide, however, are teratogenic. These metabolites do not cross the placenta. Thalidomide, however, does cross the placenta and its subsequent metabolism by the fetus results in the production of the toxic metabolites. (McIntyre J and Choonara I. Drug toxicity in the neonate. 2004 Biol of the Neonate 86:218-221)

**Wednesday, October 20, 2010****Question:**

Numerous studies have shown that a variety of manufactured and natural organic compounds such as pharmaceuticals, steroids, surfactants, flame retardants, fragrances, plasticizers and other chemicals often associated with wastewaters have been detected in the vicinity of municipal wastewater discharges. What are the five most frequently detected of such chemicals in untreated surface water sources of drinking water?

**Answer:**

The five most frequently detected chemicals in surface water were: cholesterol (59%, natural sterol), metolachlor (53%, herbicide), cotinine (51%, nicotine metabolite), <sup>2</sup>-sitosterol (37%, natural plant sterol), and 1,7-dimethylxanthine (27%, caffeine metabolite); and in ground water: tetrachloroethylene (24%, solvent), carbamazepine (20%, pharmaceutical), bisphenol-A (20%, plasticizer), 1,7-dimethylxanthine (16%, caffeine metabolite), and tri (2-chloroethyl) phosphate (12%, fire retardant).(Focazio MJ, et al. A national reconnaissance for pharmaceuticals and other organic wastewater contaminants in the US-II Untreated drinking water sources. 2008 Sci Total Env 402(2-3):201-216)

**Tuesday, October 19, 2010****Question:**

What role does "binge drinking" play with regard to the epidemiology of alcohol use in the USA?

**Answer:**

Excessive alcohol use is the third leading preventable cause of death in the US. It accounts for an annual average of approximately 79,000 deaths and over 2.25 million years of potential life lost (YPLL). Binge drinking was responsible for more than 50% of these deaths and two thirds of the total YPLL. (MMWR October 8,2010, 59(39):1274-1279)

**Monday, October 18, 2010****Question:**

Unprotected occupational exposure to benzene has, under certain circumstances of heavy exposure for prolonged periods of time, been associated with the development of acute myelogenous leukemia (AML) in some cases. Tobacco smoke is known to contain benzene. What is the current thinking with regard to the association between AML and tobacco smoke?

**Answer:**

The cited reference points out that an association between cigarette smoking and AML has not been a universal finding. However, over the past two decades, the majority of studies have indeed reported a statistically significant, moderate relationship with a relative risk of about 1.4 for AML among cigarette smokers compared to nonsmokers and the relative risk approaches 2.0 for heavy smokers. In 2004, the US Surgeon General and the International Agency on Research in Cancer of the World Health Organization each concluded, based on the data available, that cigarette smoking does indeed cause AML. (Lichtman MA. Cigarette smoking, cytogenetic abnormalities and acute myelogenous leukemia. 2007 Leukemia 21:1137-1140)

**Friday, October 15, 2010****Question:**

Dimercaprol, also known as BAL or "British Anti-Lewisite", is a chelating agent that is found on most hospital formularies. BAL is commonly recommended for the treatment of which three poisonings and what are the commonly recognized complications of the use of this drug?

**Answer:**

Dimercaprol is used for the treatment of arsenic, gold and mercury poisoning. This agent causes pain on injection, fever in approximately 30% of children and an increase in blood pressure associated with tachycardia. (The Medical Letter Sept 20,2010, 52(1347):75-76)

**Thursday, October 14, 2010****Question:**

What are "poppers" and what is the potential retinal toxicity related to the use of these substances?

**Answer:**

According to the cited reference, Poppers (slang for various forms of alkyl nitrite) are volatile nitric oxide donors that have been used for decades as recreational drugs." These authors report prolonged visual loss as a result of damage to foveal photoreceptors shortly after inhaling poppers. The authors of the cited reference detected isopropyl nitrite (a very potent nitric oxide donor) in the vapors from "popper" vials. They indicated "it is likely that the visual symptoms were due to acute, massive release of nitric oxide. Nitric oxide modulates photoreceptor metabolism and function. It also activates guanylate cyclase 4, a key enzyme for recovery of photoreceptor function after phototransduction. They reported Retinal damage was functionally and anatomically limited to the foveal center, a situation similar to that observed in photic injury. Experimentally, nitric oxide is indeed known to contribute to photic injury. Because nitric oxide is a potent vasodilator, acute changes in ocular perfusion pressure might have contributed to retinal damage. (Audo I, et al. Poppers-associated retinal toxicity. 2010 NEJM 363:1583-1585)

**Wednesday, October 13, 2010****Question:**

What is fly ash?

**Answer:**

Fly ash is the solid material carried away from power plant boilers in the flue gas during coal combustion. The properties of fly ash vary with several factors including geographic origin of the source coal, conditions during combustion and sampling position in the power plant. Typical fly ash consists of spherical particles embedded in amorphous matrices. The major elemental constituents of fly ash are Si, Fe, Al, Ca, C, Mg, K, Na, S, Ti, P and Mn. (el-Mogazi D, et al. A review of physical, chemical, and biological properties of fly ash and effects on agricultural ecosystems. 1988 Sci Total Env 74:1-37)

**Tuesday, October 12, 2010****Question:**

Dear friends The AACT "Question of the Day" will be on a brief hiatus during the course of this weeks North American Congress of Clinical Toxicology (NACCT). The Question of the Day will resume on Wednesday, October 13,2010. Thank you.

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**Thursday, October 7, 2010****Question:**

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**Answer:**

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#### Wednesday, October 6, 2010

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#### Tuesday, October 5, 2010

##### Question:

What is the major clinical difference between tick paralysis that is seen in Australia (usually caused by Ixodes holocylus ticks) and cases of tick paralysis occurring in North America (usually caused by Dermacentor andersoni and D variabilis ticks)?

##### Answer:

In cases of tick paralysis reported in Australia the clinical symptoms often progress for 24-48 hours after tick removal whereas tick paralysis reported in North American usually begins to remit as soon as the tick is removed. (Edlow J and McGillicuddy D. Tick paralysis. 2008 Infect Dis Clin N Am 22:397-413.

#### Monday, October 4, 2010

##### Question:

What are the generally recognized neuro-imaging abnormalities associated with long term abuse of inhaled toluene?

##### Answer:

The evidence from the neuroimaging literature consistently supports the notion of long-term harms from chronic toluene abuse with evidence of diffuse atrophy of the cerebrum, cerebellum and brainstem, sulcal widening, and ventricular dilation.(Yucel M, et al. Toluene misuse and long-term harms: A systematic review of the neuropsychological and neuroimaging literature. 2008 Neuroscine and Biobehavioral Rev. 32:910-926)

#### Friday, October 1, 2010

##### Question:

What non-invasive study can be used to estimate the concentration of lead in bone?

##### Answer:

Bone lead concentration is measured using a technique known as x-ray fluorescence. This technique can provide a non-invasive estimate of cumulative lead exposure by determining the amount of lead in bone (typically the tibia). (Morrow L, et al. Past occupational exposure to lead: Association between current blood lead and bone lead. 2007 Arch Env Occ Health, 62(4):183-186)

#### Thursday, September 30, 2010

##### Question:

Methyl mercury (MeHg) poisoning of individuals living near Minamata Bay on the southwestern coast of Kyushu island, Japan, was reported beginning in the early 1950s. This epidemic focused awareness regarding the severe neurological problems that can result from MeHg poisoning. What are the clinical manifestations of acute methyl mercury poisoning?

##### Answer:

The cited article points out that acute adult cases of methyl mercury poisoning may present with findings including: blurred vision, hearing impairment, olfactory and gustatory disturbances, ataxic gait, clumsiness of the hands, dysarthria, and somatosensory and psychiatric disorders. Children born to mothers exposed to MeHg show extensive spongiosis of the cerebral cortex. (Ekino S, et al. Minamata disease revisited: An update on the acute and chronic manifestations of methylmercury poisoning. 2007 J Neurol Sci 262:131-144)

#### Wednesday, September 29, 2010

##### Question:

The feared venomous snake Bothrops lanceolatus (one species of Fer de Lance) is endemic to which Caribbean island? What characterizes the envenoming by this species?

##### Answer:

Bothrops lanceolatus (Fer de lance) is an endemic species confined to the Island of Martinique in the Caribbean. Other Bothrops species exist in other locals including the tropical forests of Venezuela, Colombia, Peru, Ecuador, Brazil, Bolivia and northern Argentina, Central America, and possibly Mexico. However, B. lanceolatus is essentially limited to Martinique. Envenoming by this species leads to local effects and occasionally systemic symptoms which may include thrombocytopenia and disseminated intravascular coagulation. Araujo A et al. Coagulant and anticoagulant activities of Bothrops lanceolatus (Fer de lance) venom. 2001 Toxicon 39:371-375)

#### Tuesday, September 28, 2010

##### Question:

What was "Operation Ranch Hand"?

##### Answer:

"Operation Ranch Hand" was the name given to the defoliant spraying activities carried out by the US Air Force during the Vietnam War during the years 1962 through 1971. (Young AL, et al. Environmental fate and bioavailability of agent orange and its associated dioxin during the Vietnam War. 2004 Environ Sci & Pollut Res 11(6):359-370)

#### Monday, September 27, 2010

##### Question:

Hydroxycobalamin is a vitamin B 12 precursor used as an antidote for cyanide poisoning. What are the reported clinical manifestations of allergic reactions to this antidote?

##### Answer:

The reported clinical manifestations of allergic reactions to hydroxycobalamin include chest tightness, edema, urticaria, pruritis, dyspnea and rash. (Fortin J, et al. Hydroxycobalamin for poisoning caused by ingestion of potassium cyanide: a case study. 2010 J Emer Med 39(3):320-324)

#### Friday, September 24, 2010

##### Question:

Mees' lines (also known as Aldrich or Reynolds' lines) are transverse white bands on the nail plate laid down during periods of stress. Mees' lines are indicative of systemic pathology and may serve as a useful guide to diagnosis for clinicians. What are the common clinical associations with Mees lines (both toxicologic and non-toxicologic)?

##### Answer:

Common toxicological associations include poisoning with arsenic or thallium as well as clinical fluorosis. Non toxicological associations include severe infection, renal disease, cardiac failure, and malignant disease. (Chauhan S, et al. Mees lines. 2008 The Lancet, 372(9647):1410.

#### Thursday, September 23, 2010

##### Question:

Vancomycin is known to cause two types of hypersensitivity reactions, what are they?

##### Answer:

The two types of hypersensitivity reactions associated with vancomycin are the so-called "red man syndrome" and anaphylaxis. Red man syndrome is an infusion-related reaction peculiar to vancomycin. It typically consists of pruritus, an erythematous rash that involves the face, neck, and upper torso. (Sivagnanam and Deleu D. Red man syndrome. 2003 Crit Care 7:119-120)

#### Wednesday, September 22, 2010

##### Question:

Hypersensitivity pneumonitis (HP) is an immunologically induced lung disease caused by repeated inhalation of various agents in sensitized individuals. One group of professional musicians has recently been identified as possibly being at risk for the development of HP. What is the proposed cause for this newly described malady and what group of musicians are involved?

**Answer:**

Brass wind instruments contaminated with a variety of mold species have been implicated as possibly being associated with the development of HP in some musicians. (Metersky, ML et al. Trombone players lung: A probable new cause of hypersensitivity pneumonitis, 2010 Chest 138:754-756)

**Tuesday, September 21, 2010****Question:**

When was Fetal Alcohol Syndrome (FAS) first described?

**Answer:**

Fetal alcohol syndrome, the most severe manifestation of the adverse effects of alcohol on fetal development, was first described in the French medical literature by Lemoine et al. in 1968 [Les enfants des parents alcooliques: anomalies observes a propos de 127 cas (The children of alcoholic parents: anomalies observed in 127 cases). Quert in Medicine 8, 476482] (Calhoun F and Warren K. Fetal alcohol syndrome: Historical perspectives. 2007 Neurosci Bio-behavioral Rev, 31:168-171)

**Monday, September 20, 2010****Question:**

What is Burton's Line?

**Answer:**

The reaction of circulating lead with sulfur ions released by oral microbial activity may cause the deposition of lead sulfide at the interface of the teeth and gums, referred to as Burton's line. (Santiago Nogué S and Culla, A. 2006 N Engl J Med, 354:e21May 18, 2006)

**Thursday, September 16, 2010****Question:**

Pneumomediastinum is a rare complication associated with the use of cocaine. What is the proposed mechanism for the development of cocaine associated pneumomediastinum?

**Answer:**

The mechanism of cocaine-induced pneumomediastinum is believed to be secondary to barotrauma resulting from the inhalation technique or from severe cough triggered by the inhaled agent. It is more common with free base cocaine crack than the intranasal form and not reported with intravenous use. (Alnsa M, et al. Clinical course and outcome of cocaine induced pneumomediastinum. Am J Med Sci 2010;339(1):6567.

**Wednesday, September 15, 2010****Question:**

What spider is known as the most dangerous spider in the world based on lethal dose studies conducted in animals?

**Answer:**

The Australian funnel-web spiders (Atrax and Hadronyche spp., Hexathelidae) are known as the most dangerous spider in the world based on lethal dose studies conducted in animals. (Vetter RS and Isbister GK. Medical aspects of spider bites. 2008 Annu Rev Entomol, 53:409-429)

**Tuesday, September 14, 2010****Question:**

Nephrogenic systemic fibrosis (NSF) is a rare, but serious side effect associated with the use of agents known as GBCAs among certain patients with kidney disease. What are GBCAs?

**Answer:**

Gadolinium-based contrast agents (GBCAs) are intravenous drugs used in diagnostic imaging procedures to enhance the quality of magnetic resonance imaging (MRI) or magnetic resonance angiography (MRA). NSF has not been reported in patients with normal kidney function. Patients at greatest risk for developing NSF after receiving GBCAs are those with impaired elimination of the drug, including patients with acute kidney injury or chronic, severe kidney disease (with a glomerular filtration rate or GFR < 30 mL/min/1.73m2). Higher than recommended doses or repeat doses of GBCAs also appear to increase the risk for NSF. (<http://www.fda.gov/Drugs/DrugSafety/ucm223966.htm> FDA Drug Safety Communication: New warnings for using gadolinium-based contrast agents in patients with kidney dysfunction

**Monday, September 13, 2010****Question:**

What is "Chinese Chalk" also known as "Miraculous Chalk"?

**Answer:**

"Chinese Chalk" or "Miraculous Chalk" is an insecticide that comes in the form of a chalk. It is mostly imported illegally from China and often bears a label in both English and Chinese. Sometimes, the manufacturer makes claims that the chalk is "harmless to human beings and animals" and "safe to use." These claims are untrue and dangerous. Because insecticide chalk looks just like regular chalk, children often take it in their hands, write with it and put it in their mouths. The active ingredient in Insecticide Chalk is deltamethrin a pyrethroid that can manifest neurotoxicity under certain circumstances. (<http://www.epa.gov/pesticides/health/illegalproducts/chalk.htm>)

**Friday, September 10, 2010****Question:**

A variety of ocular complications have been reported in individuals who smoke crack cocaine and/or methamphetamine. What are the corneal complications usually recognized and what are the postulated mechanisms for corneal pathology in these patients?

**Answer:**

Corneal problems associate with smoked cocaine or methamphetamine have been reported to include epitheliopathy, microbial keratitis, and frank corneal perforation. Four mechanisms have been hypothesized as follows. 1- cocaine/methamphetamine smoke may exert a direct toxic effect on the cornea by damaging epithelial plasma membranes and microvilli. 2- Repeated exposure to cocaine or methamphetamine smoke may result in decreased corneal sensation and poor blink reflex. 3- the drugs and materials used to cut these drugs may damage corneal nerves, leading to neurotrophic keratitis. 4- the alkaline nature of, specifically, crack cocaine smoke, might result in direct chemical injury to the cornea. (Ghosh FR, et al. Corneal ulcers associated with aerosolized crack cocaine use. 2007 Cornea, 26:966-969.)

**Thursday, September 9, 2010****Question:**

Bisphosphonate-related osteo-necrosis of the jaw (BRONJ) is a significant complication of bisphosphonate treatment for metastatic bone disease, multiple myeloma, and metabolic bone diseases. Does dental implant placement increase the risk for BRONJ in patients taking bisphosphonates?

**Answer:**

The cited article points out that "Dental implant placement is not contraindicated in patients taking oral bisphosphonates", even though oral surgical procedures have been recognized as an important risk factor for BRONJ development for patients taking these drugs." The American Association of Oral and Maxillofacial Surgeons guidelines recommend a drug holiday from 3 to 6 months before dental implant placement in patients with a history of oral bisphosphonate use for greater than 3 years. (Bedogni A, et al. Oral bisphosphonate-associated osteonecrosis of the jaw after implant surgery: A case report and literature review. 2010 J Oral Maxillofac Surg 68:1662-1666)

**Wednesday, September 8, 2010****Question:**

What is mephedrone?

**Answer:**

Mephedrone is an amphetamine-like psycho-stimulant. It is a synthetic derivative of cathinone, a monoamine alkaloid found in the plant Catha edulis. Abuse of mephedrone has been implicated in the production of a syndrome of inappropriate ADH secretion associated with hyponatremia and altered mental status. (Sammiller EM et al. A harmless high? 2010 The Lancet, 376(9742):742)

**Tuesday, September 7, 2010**

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**Question:**

The antibiotics ciprofloxacin and doxycycline are not typically administered to children. Under what unusual circumstances would these antibiotics indeed be given to pediatric aged patients?

**Answer:**

Doxycycline or ciprofloxacin are recommended for children who have been exposed to aerosolized *Bacillus anthracis*. However, amoxicillin is the preferred drug for post exposure prophylaxis when susceptibility testing indicates that the particular *B. anthracis* isolate is susceptible to penicillins. In that case transition from ciprofloxacin or doxycycline to amoxicillin is recommended. (MMWR , July 23,2010; 59(RR-6))

**Friday, September 3, 2010****Question:**

What is sibutramine, what is its mechanism of action, and what are the toxicologic and adverse effects that concern clinicians with regard to this drug?

**Answer:**

Sibutramine (brand name Meridia) blocks pre-synaptic norepinephrine and serotonin reuptake consequently inducing a sensation of satiety. In 1997 fenfluramine and dexfenfluramine, two other appetite-suppressant, were removed from the market because of unexpected primary pulmonary hypertension and valvular regurgitation. Despite the fact that these clinical effects have not been observed with sibutramine, the cited reference notes increases in blood pressure (1 to 3 mm Hg) and heart rate (4 to 5 beats per minute) consistently accompany the use of the drug. The authors go on to state these findings are of concern because even modest increases in blood pressure and heart rate are known to be associated with an increased risk of cardiovascular events. While the drug has not been removed from the market to date, the cited article states given that sibutramine has minimal efficacy for weight loss, no apparent benefit for clinical outcomes, a worrisome cardiovascular risk profile, and a plausible mechanism to explain the cardiovascular risk, it is difficult to discern a credible rationale for keeping this medication on the market. (Curfman GD, et al. Sibutramine-another flawed diet pill. 2010 NEJM 363:972-974)

**Thursday, September 2, 2010****Question:**

What is "cocktail purpura"?

**Answer:**

"Cocktail purpura" refers to a decidedly uncommon form of immune thrombocytopenia induced by quinine in tonic water or in an aperitif. (Aster RH and Bougie DW. Drug-induced immune thrombocytopenia. 2007 NEJM; 357:580-587)

**Wednesday, September 1, 2010****Question:**

The insulin sensitizing agent rosiglitazone has undergone intense scrutiny over the past several years with regard to its association with an increased risk of disease. What organ system is involved?

**Answer:**

Concordant evidence from a variety of studies indicates that rosiglitazone is associated with an increased risk for cardiovascular toxicity in the form of increased risk for myocardial ischemia. (Rosen CJ. Revisiting the rosiglitazone story- Lessons learned. 2010 NEJM published online July 21,2010)

**Tuesday, August 31, 2010****Question:**

The first symptoms of small pox constitute the so-called "prodrome phase" of the disease and may last for 2 to 4 days. What symptoms are to be expected during this prodromal phase?

**Answer:**

The first symptoms of smallpox include fever, malaise, head and body aches, and sometimes vomiting. The fever is usually high, in the range of 101 to 104 degrees Fahrenheit. At this time, people are usually too sick to carry on their normal activities. (<http://www.bt.cdc.gov/agent/smallpox/overview/disease-facts.asp>)

**Monday, August 30, 2010****Question:**

Inhalation and cutaneous anthrax are occupational hazards for certain workers in certain industries. What are they?

**Answer:**

Inhalation and cutaneous anthrax are occupational hazards for workers who process hides, hair (especially from goats), bone and bone products, and wool as well as for veterinary, agriculture and wildlife workers who handle infected animals. (MMWR "Use of Anthrax vaccine in the United States" July 23,2010, 59(RR-6))

**Friday, August 27, 2010****Question:**

Why must the anthrax vaccine be administered with special caution in persons known to be allergic to latex?

**Answer:**

Because the vaccine vial stopper used in the packaging of the anthrax vaccine contains dry, natural rubber, caution should be used when administering the vaccine to persons with known latex allergy. Epinephrine, as well as standard resuscitation drugs and equipment, should be readily available to treat anaphylaxis if it should occur in this setting. (Use of anthrax vaccine in the United States. MMWR July 23,2010; 59(RR-6):1-30).

**Thursday, August 26, 2010****Question:**

In Southern Arabia and Eastern Africa, qat (also called Khat) chewing is a widely practiced socio-cultural habit. It consists of placing the green-leaved plant into the mucobuccal fold and chewing it for several hours, with subsequent release of psychoactive agents. Qat chewing is often accompanied by smoking tobacco. The reported prevalence of qat chewing in Europe and North America is on the increase with global migration. What are the oral diseases that have been associated with qat chewing?

**Answer:**

The oral diseases reportedly associated with qat chewing include peri-odontitis, oral leukoplakia and oral cancer. Qat tends not to discolor the oral mucosa as seen in betel nut chewing. Fluorosis of enamel is a common finding in the qat chewing population but the etiology for this is generally thought to be the high fluoride concentration in drinking water in rural areas of qat growing countries. The fluoride content in qat has been shown to be low. (El-Wajeh Y and Thornhill MH. Qat and its health effects. 2009 Br Dental J 206(1):17-21)

**Wednesday, August 25, 2010****Question:**

Because most thiazide diuretics have a half-life of approximately 8 to 12 hours, once- daily dosing for this drug can be effective. Which thiazide diuretic has the longest elimination half-life?

**Answer:**

Chlorthalidone is a uniquely long-acting thiazide, with an elimination half- life ranging from 50 to 60 hours, owing to its large volume of distribution. (Ernst ME and Moser M. Use of diuretics in patients with hypertension. 2009 NEJM 361:2153-2164)

**Tuesday, August 24, 2010****Question:**

When the action of the cytochrome CYP3A is inhibited by an interacting drug, how long does that inhibition typically last?

**Answer:**

The inhibition of CYP3A by other drugs is usually reversible, typically within two to three days, once the interacting drug is discontinued. In the case of some inhibitors (e.g., diltiazem, macrolide antibiotics, mifepristone, and delavirdine), however, the effect may last much longer, because CYP3A is destroyed and new CYP3A enzyme must be synthesized. (Wilkinson GR. Drug metabolism and variability among patients in drug response, 2005 NEJM 352:2211-2221)

**Monday, August 23, 2010**



**Question:**

The known neurotoxic effects of  $\beta$ -lactam antibiotics such as cephalosporins include slurred speech, tremor, encephalopathy, seizures, mental status changes, myoclonus, asterixis, nonconvulsive status epilepticus, and coma. Which patients are at highest risk for the development of cephalosporin-associated neurotoxicity?

**Answer:**

Those at highest risk include patients with renal insufficiency/renal failure, those with prior neurologic disease, and the elderly. (Grill MF and Maganti R. Cephalosporin-induced neurotoxicity: Clinical Manifestations, potential pathogenic mechanisms, and the role of electroencephalographic monitoring. 2008 Ann Pharmacotherapy; 42:1843-1850)

**Friday, August 20, 2010****Question:**

In clinical practice, several markers of chronic alcohol abuse are employed to determine post mortem evidence of chronic alcohol use. These markers have included serum gamma-glutamyltransferase (c-GT) and aminotransferase (ALT, AST) levels and mean corpuscular volume (MCV). Studies have illustrated the poor specificity and sensitivity of these markers and their unsuitability for autopsy material due to post-mortem instability. What new markers have been proposed for the post mortem determination of chronic alcohol use in deceased subjects?

**Answer:**

These markers have included carbohydrate-deficient transferrin (CDT), fatty acid ethyl esters (FAEEs), fatty acid methyl esters (FAMES), ethylglucuronide (EtG), phosphatidylethanol (PEth), 5-hydroxytryptophol to 5-hydroxyindole-3-acetic acid (5-HTOL/5-HIAA) ratio, sialic acid, beta-hexosaminidase, blood acetate, acetaldehyde adducts, and dolichol. (Rainio J, et al. Objective post-mortem diagnosis of chronic alcohol abuse- A review of studies on new markers. 2008 Legal Medicine, 10:229-235)

**Thursday, August 19, 2010****Question:**

What are the long term (chronic) adverse health effects of the anthrax vaccine?

**Answer:**

The U.S. Dept. of Defense has published several studies evaluating long-term health effects among vaccinated and unvaccinated military personnel. Additional studies have assessed the long-term health of vaccinated researchers and fertility parameters for vaccinated males. None of the studies to date have found the risk for adverse health effects or chronic disease (e.g. cancer or infertility) was higher after anthrax vaccination. (MMWR July 23,2010; 59(RR-6):1-30)

**Wednesday, August 18, 2010****Question:**

Modafinil (Provigil) is a benzhydryl sulfinyl acetamide first approved by FDA in 1998 for the treatment of excessive daytime sleepiness associated with narcolepsy. In 2004 additional indications for this drug were approved by the FDA. What are these additional indications?

**Answer:**

In 2004 the additional indications for modafinil included excessive daytime sleepiness due to obstructive sleep apnea/hypopnea syndrome (OSAHS) and shift work sleep disorder (SWSD). (The Medical Letter, August 9,2010, 52(1344):61)

**Tuesday, August 17, 2010****Question:**

Shiga toxin-producing E. coli (STEC) cause approximately 100,000 illnesses, 3,000 hospitalizations, and 90 deaths annually in the United States. Most STEC infections in the United States are caused by E. coli O157:H7, with an estimated 73,000 cases occurring each year. What media is best used to isolate this organism in the lab?

**Answer:**

Most O157 STEC isolates can be readily identified in the laboratory when grown on sorbitol-containing selective media because O157 STEC cannot ferment sorbitol within 24 hours. However, many clinical laboratories do not routinely culture stool specimens for O157 STEC. In addition, selective and differential media are not available for the culture of non-O157 STEC, and even fewer laboratories culture stool specimens for these bacteria than for O157 STEC.(Gould LH. Recommendations for diagnosis of shiga toxin-producing E. coli by clinical labs. MMWR, October 16,2009; 58(RR12):1-14.

**Monday, August 16, 2010****Question:**

Aseptic meningitis is an uncommon adverse drug reaction that has been reported in association with non-steroidal anti-inflammatory agents as well as with a variety of miscellaneous drugs. What characterizes aseptic meningitis associated with the drug trimethorim-sulfamethoxazole (TMP-SMX)?

**Answer:**

Data collected from the literature show that the symptoms due to TMP-SMX-induced aseptic meningitis begin within hours following ingestion of the drug and that there is a direct relationship between symptoms and the total amount of drugs consumed or the number of times the patient has previously received the drug. (Capra C. et al. trimethorim-sulfamethoxazole-induced aseptic meningitis: case report and literature review .2000 Intenmsive Care Medicine; 26:212-214)

**Friday, August 13, 2010****Question:**

Alcoholism is a risk factor for osteoporotic fractures and low bone density, but what are the effects of moderate alcohol consumption on bone?

**Answer:**

Compared with abstainers and heavier drinkers, persons who consume 0.5 to 1.0 drink per day have a lower risk of hip fracture. Although available evidence suggests a favorable effect of alcohol consumption on bone density, a precise range of beneficial alcohol consumption cannot be determined. (Berg KM,et al. Association between alcohol consumption and both osteoporotic fracture and bone density. 2008 Am J Med 121(5):406-418)

**Thursday, August 12, 2010****Question:**

Temperature related dysesthesia is a phenomenon reported with ciguatera fish poisoning. What other fish related poisoning is also reported to be associated with temperature related dysesthesia?

**Answer:**

Neurotoxic shellfish poisoning (NSP), which is caused by human consumption of shellfish contaminated with brevetoxin may also associated with temperature related dysesthesia. (Friedman MA, et al. Ciguatera fish poisoning: treatment, prevention and management. 2008 Marine Drugs 6:456-479)

**Tuesday, August 10, 2010****Question:**

What is bronchiolitis obliterans?

**Answer:**

Bronchiolitis obliterans (BO) is a pathologic process involving inflammation and fibrosis, primarily of the bronchioles leading to airflow obstruction. (Markopoulou K, et al. Obliterative bronchiolitis: varying presentations and clinicopathologic correlation. 2002 Eur Respir J 19:20-30.clinicopathologic

**Monday, August 9, 2010****Question:**

What are the determinants of chronic beryllium disease (CBD)?

**Answer:**

The cited reference points out that obviously a medically important exposure and dose of beryllium is necessary for development of CBD; however, differential susceptibility to CBD clearly has a genetic component. The genetic basis of immunologic reactivity to beryllium involves human leukocyte antigens (HLA); the beryllium-induced proliferation of T lymphocytes from lungs of CBD patients can be blocked by antibodies directed against the DP subgroup of HLA. In addition the nature of the beryllium exposure forms an important determinant for CBD. (Beryllium: A modern industrial hazard. Kreiss K. et al. 2007 Annu Rev Public Health 28:259-277)

**Friday, August 6, 2010**

**Question:**

Penis size has been a source of anxiety for some men through history, and even today some men may feel a need to enlarge their penises to improve self-esteem or to satisfy and/or impress their partners. Non medical personnel and patients alike have used a variety of unproven substances administered by injection into the penis to attain the wished for penile enlargement. What substances have been used and what sorts of toxicity has been manifested by this practice?

**Answer:**

Paraffin, mineral oil, metallic mercury, silicon, pe- troleum jelly, subcutaneous stone implantation, vase- line, autologous fat and cod liver oil are some of the various materials that have been tried. Some of the complications reported have included severe Fourniers gangrene, erectile dysfunction, abscess formation, granuloma formation and systemic mercury toxicity(following mercury injection). (Al-Ansari AA, et al. Subcutaneous cod liver oil injection for penile augmentation. 2010 Urology 75:1181-1184)

**Thursday, August 5, 2010****Question:**

When should clinicians be vigilant regarding the use of tetracycline antibiotics with regard to their propensity to cause renal insufficiency?

**Answer:**

Tetracycline antibiotics, with the exceptions of doxycycline and perhaps minocycline, can exacerbate renal impairment in patients with pre-existing kidney disease, and clinicians should not administer these drugs to patients with renal impairment. (Miller CS. Tetracycline-induced renal failure after dental treatment. 2009 JADA 140:56-60)

**Wednesday, August 4, 2010****Question:**

What is the risk for suicide related events in epileptics taking anti-epileptic drugs?

**Answer:**

The cited reference reported on a large number of patients and found that the use of anti-epileptic drugs was not associated with an increased risk for suicide related events in patients with epilepsy. However the authors also report anti-epileptic drug use was associated with an increased risk for suicide related events in persons diagnosed with depression and among those without epilepsy, depression or bipolar disease. (Arana A, et al. Suicide related events in patients treated with anti-epileptic drugs. 2010 NEJM; 363(6):542-551)

**Tuesday, August 3, 2010****Question:**

What are the legal requirements for the sale or purchase of drug products containing pseudoephedrine, ephedrine and phenylpropanolamine?

**Answer:**

The Combat Methamphetamine Epidemic Act of 2005 has been incorporated into the Patriot Act signed by President Bush on March 9, 2006. The act bans over-the-counter sales of cold medicines that contain the ingredient pseudoephedrine, which is commonly used to make methamphetamine. The sale of cold medicine containing pseudoephedrine is limited to behind the counter. The amount of pseudoephedrine that an individual can purchase each month is limited and individuals are required to present photo identification to purchase products containing pseudoephedrine. In addition, stores are required to keep personal information about purchasers for at least two years. (<http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm072423.htm>)

**Monday, August 2, 2010****Question:**

There are three recognized forms of anthrax infection based on route of exposure to anthrax spores: cutaneous, inhalational and gastrointestinal. Which of these routes of exposure have resulted in anthrax infection associated with exposure to the musical drums fashioned from animal hides?

**Answer:**

All three forms of anthrax have resulted from exposure derived from musical drums made from animal hides. A recent report described the extremely rare occurrence of gastrointestinal anthrax in a 24 year old woman who had participated in a drumming event where drums made from animal hides were played at a community gathering. (July 23,2010 MMWR, 59(28):872-877)

**Friday, July 30, 2010****Question:**

What is the toxin responsible for ciguatera poisoning and from where is this toxin derived?

**Answer:**

The toxin is ciguatoxin and it is derived from dinoflagellates of the genus Gambierdiscus. These grow mainly in association with macroalgae in coral reefs in tropical and subtropical climates. The toxin is transferred through the food web as the algae is consumed by herbivorous fish, which are consumed by carnivorous fish, which are then consumed by humans. (Friedman MA, et al Ciguatera fish poisoning: Treatment, prevention and management. 2008 Marine Drugs; 6:456-479)

**Thursday, July 29, 2010****Question:**

What is glyphosate and how does this chemical act to kill plants?

**Answer:**

Glyphosate is a nonselective herbicide commonly used worldwide. Glyphosate acts by inhibiting the shikimate metabolic pathway in plants. Since this pathway does not exist in humans, glyphosate is generally believed to be of very low toxicity in humans. Nonetheless, glyphosate ingestions have been reported to cause serious consequences in some cases where very large doses were ingested, often with suicidal intent. (Chen Y, et al. The epidemiology of glyphosate-surfactant herbicide poisoning in Taiwan, 1986-2007; a poison center study. 2009 Clin Tox 47(7):670-677)

**Wednesday, July 28, 2010****Question:**

What is cornpicker's eye?

**Answer:**

This occupationally related disorder occurs when mechanized combines are used to harvest corn and cornstalks. During this process, it is possible for co-existing dried Datura plants to be pulverized into a dust containing belladonna alkaloids from the Datura. This dust can become airborne and come into contact with the eyes of nearby workers causing mydriasis and possibly systemic anticholinergic symptoms as well. (Krenzelok E. Datura poisoning. 48(2):104-110)

**Tuesday, July 27, 2010****Question:**

What is acrodynia and what are the clinical symptoms associated with this problem?

**Answer:**

Acrodynia is a childhood affliction with symptoms that may include painful, red, swollen fingers and toes. One or all of these symptoms may occur in conjunction with photophobia, irritability, asthenia and hypertension. Acrodynia is believed to be a hypersensitivity reaction to mercury that was, in the past, usually caused by exposure to mercuric and mercurous salts. Clarkson TW, et al. The toxicology of mercury- Current exposures and clinical manifestations. 2003 NEJM 349(18):1731-1737)

**Monday, July 26, 2010****Question:**

Recently the FDA approved tranexamic acid (Lysteda) for the treatment of abnormally heavy menstrual bleeding (menorrhagia). What is the history of this drug and what is the mechanism of action for this drug?

**Answer:**

Tranexamic acid has been used in the US since the late 1980's to treat hemophiliacs undergoing dental extractions. It has been used in Europe for many years for the treatment of menorrhagia and is even available without prescription in some countries. Females with abnormally heavy menstrual bleeding have elevated levels of tissue plasminogen activator (tPA) and tranexamic acid is thought to reduce endometrial tPA activity. This results in decreased blood loss. In addition, it blocks lysine binding sites on plasminogen molecules thus preventing plasmin formation and menstrual fluid fibrinolysis. (The Medical Letter 52(1342) July 10,2010)

**Friday, July 23, 2010**

**Question:**

Cigarette smoking is the most common cause for lung cancer and lung cancer is the most common cancer in the world. What percentage of smokers actually get lung cancer?

**Answer:**

Interestingly, less than 20% of smokers actually get lung cancer. Unfortunately it is not yet possible to predict which smokers are most susceptible to developing lung cancer. (Hecht SS. Cigarette smoking and lung cancer: chemical mechanisms and approaches to prevention. 2002 Lancet Oncology 3:461-469)

**Thursday, July 22, 2010**

**Question:**

One very uncommon side effect of the drug chloroquine is the development of loss of pigmentation of the hair. How long must one usually take chloroquine before this very rare side effect manifests?

**Answer:**

This reversible side effect of chloroquine usually takes at least three months of daily use of more than 500 mg per day to manifest. However, this phenomenon has been observed in some cases much more quickly than three months. (Donovan J and Price V. Chloroquine induced hair hypopigmentation.2010 NEJM 363(4):372)

**Wednesday, July 21, 2010**

**Question:**

What is a "biological passport"?

**Answer:**

A biological passport monitors an athletes blood and body chemistry values over time. The goal is to assess if there has been a deviation from an established baseline to thus provide indirect detection of illegal doping. The biological passport was implemented by the International Cycling Union for the 2008 cycling season and approved for widespread use by the World Anti-Doping Agency (WADA) in 2009. Traditional testing compares, for example, concentrations of a banned substance with population averages while the biological passport emphasizes many readings from the same athlete, presumably making it easier to spot subtle patterns in a given individual. (Wozny M. The biological passport and doping in athletics. 2010 The Lancet 376(9735):79)

**Tuesday, July 20, 2010**

**Question:**

Are material safety data sheet documents (MSDS) useful in the diagnosis and management of occupational contact dermatitis?

**Answer:**

One paper recently addressed this very question and concluded that MSDS are inadequate for the protection and diagnosis of workers with suspected OCD. Sensitizers are frequently omitted from MSDS documents and clinicians may be unsuccessful in obtaining crucial information from manufacturers via their MSDS documents.(Keegel T., et al. Are material safety data sheet documents (MSDS) useful in the diagnosis and management of occupational contact dermatitis? 2007 Contact Derm 57(5):331-336)

**Monday, July 19, 2010**

**Question:**

Mainstream cigarette smoke has been identified as a major causative agent for the development of lung cancer. Four major histological classifications for lung cancer have been identified: squamous cell carcinoma (SQC), small cell carcinoma (SCLC), large cell cancer (LGC) and adenocarcinoma (ADC). Does cigarette smoking increase the risk for all four histological types of lung cancer?

**Answer:**

The cited study indicates that the association may be stronger with squamous cell carcinoma (SQC) and small cell carcinoma (SCLC) than with large cell cancer (LGC) and adenocarcinoma (ADC). Nevertheless, cigarette smoking is a very strong risk factor for all four types of lung cancer. (Khuder SA. Effect of cigarette smoking on major histologic types of lung cancer: a meta-analysis. 2001 Lung Cancer, 31:139-148)

**Friday, July 16, 2010**

**Question:**

Part II (see Thursdays Question of the Day) What is the recommended initial emergency treatment for white phosphorus burns?

**Answer:**

The recommended emergency treatment for white phosphorus burns includes careful removal and protected storage of the patient's clothing and continuous irrigation with water. Easily identifiable fragments of white phosphorus should be sterilely derided and properly disposed of. The use of a Woods lamp may facilitate identification of retained particles containing white phosphorus. In addition, the use of a copper sulfate solution (0.5%) may be used to immerse exposed extremities to reduce the burning process and facilitate particle removal. (Al Barqouni, et al. White phosphorus burn. 2010 The Lancet 376:68)

**Thursday, July 15, 2010**

**Question:**

This will be a two part Question of the Day. Part II to follow tomorrow. Part I: What is white phosphorus? How might contact with this chemical result in systemic injury?

**Answer:**

White phosphorus is a smoke producing, waxy, yellow transparent combustible solid used primarily in military and some industrial applications. On contact with exposed skin, white phosphorus produces painful chemical injuries. Due to high lipid solubility the injuries may extend into the deep tissues with subsequent delayed wound healing. In addition, it can also be systemically absorbed with multiple organ injury including damage to erythrocytes, kidneys, liver and heart. (Al Barqouni, et al. White phosphorus burn. 2010 The Lancet 376: 68)

**Wednesday, July 14, 2010**

**Question:**

The administration of etomidate for rapid sequence intubation (RSI) has been linked to subsequent adreno-cortical insufficiency in non-trauma patients. What is the effect of etomidate on adrenal gland function in trauma patients and what is the mechanism for the effects that etomidate may cause with regard to adrenal insufficiency in all patients?

**Answer:**

The cited study reported that the use of etomidate for RSI in trauma patients led to chemical evidence of adrenocortical insufficiency and may have contributed to increased hospital and ICU lengths of stay. Etomidate has been shown to inhibit 11-beta-hydroxylase (in trauma and non-trauma patients alike), the enzyme responsible to catalyze the conversion of deoxycortisol to cortisol in the adrenal gland. This can lead to decreased concentrations of cortisol for at least 24 hours following the administration of etomidate. (Hildreth AN, et al. Adrenal suppression following a single dose of etomidate for rapid sequence intubation: a prospective, randomized study. J Trauma. 2008;65:573579)

**Tuesday, July 13, 2010**

**Question:**

What is the impact on air quality for communities that exist in areas adjacent to large airports and how does the impact on air quality in those communities compare with that in a typical urban environment?

**Answer:**

The cited article concluded: "For a population living in the vicinity of a large airport, risk assessment can only be achieved by relying on air monitoring data. Such data show that there is an impact on the air quality of the adjacent communities, but that impact does not result in levels higher than those in a typical urban environment". (Tesseraux I. Risk factors of jet fuel combustion products. 2004 Tox Letters 149:295-300)

**Monday, July 12, 2010**

**Question:**

Succinylcholine is the drug of choice for inducing paralysis in many instances where emergency endotracheal intubation is required. A number of acquired pathological conditions are known to have the potential to cause acute and lethal hyperkalemia with the administration of succinylcholine. What are these conditions?

**Answer:**

The acquired pathological conditions that may cause acute and potentially lethal hyperkalemia with the administration of succinylcholine include upper or lower motor neuron defects; prolonged chemical denervation as may occur in association with some muscle relaxants, magnesium and clostrial toxins; direct muscle trauma, tumor or inflammation; thermal injury; disuse atrophy; and severe infection. (Martyn J, et al. Succinylcholine-induced hyperkalemia in acquired pathologic states. 2006 Anesthesiology 104:158-169)

**Wednesday, July 7, 2010****Question:**

Sumatriptan is one of seven serotonin receptor agonists currently available in the US for the treatment of migraine headaches. Sumatriptan is the only one of this group of "triptans" currently formulated for subcutaneous injection. How does the efficacy of Sumatriptan delivered via subcutaneous injection compare with the oral and intranasal routes of delivery for this drug?

**Answer:**

The cited article points out that subcutaneous injections of sumatriptan act more rapidly than oral or intranasal routes of administration. (The Medical Letter, June 28, 2010, 52(1341):49-51.)

**Tuesday, July 6, 2010****Question:**

Cryptosporidiosis is a nationally notifiable gastrointestinal illness. What is the cause for this malady and what are the common clinical findings associated with this illness? How is this illness transmitted?

**Answer:**

Cryptosporidiosis is a gastrointestinal illness caused by protozoa of the genus *Cryptosporidium*. The cited reference points out that In otherwise healthy persons, clinical illness is characterized by watery diarrhea, which may be accompanied by abdominal cramps, decreased appetite, fever, nausea, vomiting, and weight loss. "Crypto" is transmitted by the fecal-oral route and results from the ingestion of *Cryptosporidium* oocysts through consumption of fecally contaminated food or water or through direct person to person or animal to person contact. (MMWR, June 11, 2010, 59(SS-6):1-14)

**Friday, July 2, 2010****Question:**

The TASER is a device used by many law enforcement organizations and others to deliver incapacitating electric energy to immobilize and subdue an individual. What does the acronym "TASER" stand for?

**Answer:**

TASER is an acronym for "Thomas A. Swift Electronic Rifle". This device was developed in the US by a NASA researcher in the 1960s and has actually been available commercially since 1974. (Robb M, et al. Review article: Emergency department implications of the TASER. 2009 Emerg Med Australasia 21:250-258.)

**Thursday, July 1, 2010****Question:**

What is GBL?

**Answer:**

GBL, also known as gamma butyrolactone, is a pro-drug for gamma hydroxybutyric acid (GHB). GBL has emerged as a recreational drug over the past decade. (Hefe B, et al. Fast-in, fast-out. 2009 The Lancet, 373:1398)

**Wednesday, June 30, 2010****Question:**

What is the probable increased risk for cancer associated with a single CT scan?

**Answer:**

The National Research Council (NRC) has concluded that patients exposed to radiation in the range of doses usually associated with a single CT scan have an increased risk for cancer however uncertainty remains regarding the magnitude of that risk. The recent cited editorial indicates that the risk from a single CT scan may be as high as 1 in 80. (Smith-Bindman R. Is computed tomography safe? 2010 NEJM 363(1):1-4)

**Tuesday, June 29, 2010****Question:**

What is DAWN, what agency is responsible to administer DAWN and how does DAWN work?

**Answer:**

DAWN is the Drug Abuse Warning Network administered by SAMSHA (Substance Abuse and Mental Health Services Administration). DAWN is "a public health information system that tracks the impact of drug use, misuse, and abuse in the US by monitoring drug-related hospital emergency department visits." DAWN uses a sample of EDs to "estimate national ED visits" and collects data from "a stratified, simple random sample of approximately 220 nonfederal, short stay general hospitals operating 24 hour EDs in the US." The DAWN data is designed to "produce estimates and trends [of drug use] for individual metropolitan areas and the US overall.." (MMWR, June 18, 2010, 59(23):705-707)

**Monday, June 28, 2010****Question:**

Aminoglycosides were the first class of drugs to call attention to cochlear and vestibular toxicity when streptomycin and dihydrostreptomycin were used to treat tuberculosis. How is aminoglycoside ototoxicity characterized?

**Answer:**

Aminoglycosides are associated with high-frequency sensorineural hearing loss that is permanent and bilateral. (Guthrie OW. Aminoglycoside induced ototoxicity. 2008 Toxicology, 249:91-96)

**Friday, June 25, 2010****Question:**

What is the ARCOS system and who reports to this important Drug Enforcement Administration initiative?

**Answer:**

ARCOS is the Automation of Reports and Consolidated Orders System put in place by the DEA to help combat drug diversion activities. Manufacturers of bulk and/or dosage form controlled substances must report inventories, acquisitions, and dispositions of all substances in Schedules I and II, and narcotic and Gamma-Hydroxybutyric Acid (GHB) substances in Schedule III (see 21 CFR §1308 Schedule of Controlled Substances). Additionally, manufacturers must report synthesizing activities involving all substances in Schedules I and II, narcotic and Gamma-Hydroxybutyric Acid (GHB) substances in Schedule III, and selected psychotropic controlled substances in Schedules III and IV (see 21 CFR § 1304.33 Reports to ARCOS). Distributors of bulk and/or dosage form controlled substances as well must report inventories, acquisitions, and dispositions of all substances in Schedules I and II, and narcotic and Gamma-Hydroxybutyric Acid (GHB) substances in Schedule III. (<http://www.deadiversion.usdoj.gov/arcons/faq.htm>)

**Thursday, June 24, 2010****Question:**

A causal relationship between prenatal maternal smoking and a variety of pre and post natal effects is currently well accepted by the scientific community. What specific pre and post natal effects are considered to be causally related to prenatal maternal smoking in applicable cases?

**Answer:**

The specific pre and post natal effects considered to be causally related to prenatal maternal smoking in applicable cases include: premature membrane rupture, placenta previa, abruptio placenta, preterm delivery, fetal growth restriction, and sudden infant death syndrome (SIDS). (Dietz P, et al. Infant morbidity and mortality attributable to prenatal smoking in the U.S. 2010 Am J Prev Med, 39(1):45-52.)

**Wednesday, June 23, 2010**

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**Question:**

Vibration (> 100 Hz) is considered by some to be an occupational "toxicant". More than 1.5 million individuals in the US engage in work that exposes them to "hand transmitted vibration" placing them at risk for the so-called "hand-arm vibration syndrome" (HAVS). What are the clinical characteristics of HAVS?

**Answer:**

The cited reference indicates that HAVS is characterized by "dysfunction of the peripheral vascular and sensorineural systems" and points out that the most common findings associated with HAVS is cold induced vasospasm and digital blanching, sometimes called "vibration white finger". (Krajnak K, et al. Characterization of frequency dependent responses of the vascular system to repetitive vibration. 2010 JOEM, 52(6):584-594)

**Tuesday, June 22, 2010**

**Question:**

Hyperkalemia is a potentially life-threatening electrolyte disorder. It is relatively common with a reported incidence of hyperkalemia generally ranging between 1.1 and 10% of hospitalized patients. What is the utility of the EKG in making a definitive diagnosis of hyperkalemia?

**Answer:**

The EKG has been widely reported to have poor sensitivity and specificity as a diagnostic test for hyperkalemia. The clinical management of hyperkalemia should be guided by serial serum potassium determinations as well as relevant clinical findings. (Montague BT, et al. Retrospective review of the frequency of EKG changes in hyperkalemia. 2008 Clin J Am Soc Nephrol 3: 324-330)

**Monday, June 21, 2010**

**Question:**

Following the ingestion of caustics, the pediatric patients symptoms and clinical signs are not always a reliable predictor of the ultimate injury and prognosis. Consequently, many pediatric patients undergo esophagoscopy. What percentage of pediatric patients without obvious oral injury will have concurrent esophageal injury and what percentage of those with oral injury will not have esophageal injury?

**Answer:**

Approximately 12% of patients without oral injury have concurrent esophageal injury, and up to 70% of oral injury can be without esophageal injury. (Riffat F and Cheng A. Pediatric caustic ingestion: 50 consecutive cases and a review of the literature. 2009 Diseases of the Esophagus, 22:89-94)

**Friday, June 18, 2010**

**Question:**

Besides nicotine, what constituents of cigarette smoke contribute to the addictive potential of cigarettes?

**Answer:**

Monoamine oxidase enzymes catalyze the metabolism of biogenic amines including dopamine, norepinephrine and serotonin. The cited reference indicates that condensation products of acetaldehyde in cigarettes smoke with biogenic amines inhibit the activity of monoamine oxidases A and B. Evidence points to the fact that monoamine oxidase may increase the addictive potential of smoking by reducing the metabolism of dopamine. (Benowitz NL. Nicotine addiction. 2010 NEJM 362(24):2295-2303)

**Thursday, June 17, 2010**

**Question:**

What drugs are currently FDA approved for the treatment of Alzheimer's disease?

**Answer:**

The cholinesterase inhibitors donepezil (Aricept), rivastigmine (Exelon) and galantamine (Razadyne) and the N-methyl-D-aspartate receptor antagonist memantine (Namenda) are the only drugs currently FDA approved for the treatment of Alzheimer's disease. (Mayeux R. Early Alzheimer's disease. 2010 NEJM 362(23):2194-2201)

**Wednesday, June 16, 2010**

**Question:**

Valproic acid use during the first trimester of pregnancy is associated with an increased risk for a variety of important congenital malformations. What are the six (6) major congenital malformations most strongly associated with the use of valproic acid during the first trimester of pregnancy?

**Answer:**

The six (6) major congenital malformations most strongly associated with the use of valproic acid during the first trimester of pregnancy are: spina bifida (OR 12.7, CI 7.7-20.7); craniostenosis (OR 6.8, CI 1.8-18.8); cleft palate (OR 5.2, CI 2.8-9.9); hypospadias (OR 4.8, CI 2.9-8.1); atrial septal defect (OR 2.5, CI 1.4-4.4) and polydactyly (OR 2.2, CI 1.0-4.5) (Jentink J, et al. Valproic acid monotherapy in pregnancy and major congenital malformations. 2010 NEJM 362(23): 2185-2193)

**Tuesday, June 15, 2010**

**Question:**

What are the two most important clinical problems related to the long-term use of inhaled corticosteroids in patients with COPD?

**Answer:**

The long-term use of inhaled corticosteroids can increase the risk of fractures and pneumonia in patients with COPD. Other potential adverse effects may include oral candida infection as well as dysphonia. Systemic absorption of inhaled steroids can induce skin bruising, cataracts and decreased bone mineral density. (The Medical Letter, May 31,2010, 52(1339):41-42)

**Monday, June 14, 2010**

**Question:**

Most of the medical problems associated with so-called button batteries occur among young children under the age of 5 years. The usual injuries reported involve ingestion into the aerodigestive tract or lodging of batteries in the nose or ear canal. The first fatal case from an ingested alkaline cell was reported in 1977. What are the potential adverse dermal effects associated with these small batteries?

**Answer:**

A few cases of dermal injury have been reported when button batteries have become lodged against the skin inside of a cast applied to an extremity. These events involved the development of local necrotic lesions at the site where the battery was lodged. (Moulton SL, et al. A wound caused by a small alkaline cell (button battery) under a plaster cast: Report of a case. 2009 J Burn Res, 30:355-357)

**Friday, June 11, 2010**

**Question:**

What is the toxin excreted by poison dart frogs in the wild and what is the mechanism of action for this toxin?

**Answer:**

Poison dart frogs (Phylllobates spp.) excrete several alkaloid toxins via their skin. Among these excretions is one of the most potent toxins known in nature, batrachotoxin (BTX). As noted in the cited reference, BTX is a potent modulator of voltage-gated sodium channels, which are key to the generation of action potentials and are critical elements in the signal transduction process of membranes of neurons and most excitable cells. VGSC modulation by BTX causes an irreversible depolarisation of nerves and muscles, fibrillation, arrhythmias and eventually cardiac failure. Aside from the above-mentioned effects, BTX causes a feeling of numbness upon contact with human tissue, an effect that remains unexplained. (Bosmans F, et al. The poison dart frogs batrachotoxin modulates Nav 1.8. 2004 FEBS Letters, 577(1-2):245-248)

**Thursday, June 10, 2010**

**Question:**

What is the mortality rate for inhalational anthrax?

**Answer:**

In the past authorities indicated that the mortality rate for inhalational anthrax ranged from 89% to 96%. However, the anthrax attacks in the US during 2001 were associated with a much reduced mortality rate (45%). This reduction in mortality has been attributed to prompt diagnosis as well as rapid initiation of therapy. (Holty JC, et al. Anthrax: A systematic review of atypical presentations. 2006 Ann Emerg Med 48(2):200-211)

**Wednesday, June 9, 2010**

**Question:**

The chemical dinitrophenol (DNP) has been used as a weight loss adjunct both licitly (in the past) and, at times, illicitly. How does this chemical promote weight loss?

**Answer:**

Weight loss (as well as toxicity) associated with the use of DNP presumably occurs due to the fact that DNP uncouples oxidative phosphorylation. (Hsiao AL, et al. Pediatric fatality following ingestion of dinitrophenol: postmortem identification of a "dietary supplement". 2005 Clin Tox, 43:281-285)

**Tuesday, June 8, 2010****Question:**

Approximately 80 coral snake bites per year are reported to US poison centers. What is the geographic range for coral snakes and which coral snakes are responsible for coral snake bite toxicity in the USA?

**Answer:**

Coral snakes are in the family Elapidae and are found in the southeastern United States, Mexico, Central and South America. Only two species (each with multiple subspecies) are responsible for all coral snake toxicity in the United States: *Micrurus fulvius fulvius* (Eastern coral snake) and *Micrurus tener* (Texas coral snake) (Morgan DL, et al. Texas coral snake (*Micrurus tener*) bites. 2007 S Med J, 100(2):152-156)

**Monday, June 7, 2010****Question:**

What is the simplest and most accurate way to identify *Loxosceles* spiders?

**Answer:**

The eye pattern is the most accurate and simplest way to identify *Loxosceles* spiders. Although most U.S. spiders have eight eyes, typically arranged in two rows of four, brown recluse spiders have six eyes arranged in pairs (dyads), with one anterior and two lateral dyads. This pattern is common to the 100 *Loxosceles* species worldwide. (Swanson DL and Vetter RS. Bites of brown recluse spiders and suspected necrotic arachnidism. 2005 NEJM 352: 700-707)

**Friday, June 4, 2010****Question:**

Approximately what percentage of brown recluse (*Loxosceles reclusa*) spider bites will lead to major post-bite problems such as unacceptable scarring, hospitalizations, chronic lesions, etc.?

**Answer:**

It is believed that less than 15% of brown recluse spider bites will result in major post-bite problems. (Wendell RP. Brown recluse spiders: A review to help guide physicians in nonendemic areas. 2003 S Med J 96(5):486-490)

**Thursday, June 3, 2010****Question:**

Bismuth containing compounds are often used as first line therapy for the eradication of gastrointestinal tract *Helicobacter pylori*. What is the safety profile of bismuth compounds used either alone or in combination with antibiotics for the treatment of *H. pylori* infection, or *H. pylori*-related diseases?

**Answer:**

The cited study is a systematic review of the question that revealed bismuth for the treatment of *H. pylori* is safe and well-tolerated. These investigators found that the only adverse event occurring significantly more commonly was dark stools. (Ford AC, et al. Adverse events with bismuth salts for *Helicobacter pylori* eradication: Systematic review and meta-analysis. 2008 World J Gastroenterol 14(48):7361-7370)

**Wednesday, June 2, 2010****Question:**

To date seven (7) sero-types (A-G) of botulinum toxin have been identified associated with food-borne botulism. Which serotypes are the most common causes for cases of human food-borne botulism?

**Answer:**

Human cases of food-borne botulism are caused most commonly by sero-types A, B and E. Occasional human cases have been caused by type F. (Witoonpanich R, et al. Survival analysis for respiratory failure in patients with food-borne botulism. 2010 Clin Tox 4(3):177-183)

**Tuesday, June 1, 2010****Question:**

Low-dose methotrexate (MTX) administration is commonly used in the treatment of ectopic pregnancy. MTX is potentially teratogenic, even following exposure to a single dose. What is the appropriate timing for safe conception following the treatment of ectopic pregnancy when MTX is used ?

**Answer:**

The cited study reports on 125 pregnancies, 45 of which occurred within 6 months after MTX treatment. The outcome of these pregnancies was compared with that of 80 pregnancies occurring 6 months or longer following MTX treatment. The fetal malformation and adverse outcome rates for both groups were similar (odds ratio 1.003, 95% CI 0.981.02). The authors reported that the interval between the last MTX treatment for ectopic pregnancy had no effect on the outcome of the pregnancy that shortly followed it. (Svirsky R, et al. The safety of conception occurring shortly after methotrexate treatment of an ectopic pregnancy. 2009, Reproductive Tox, 27:85-87)

**Monday, May 31, 2010****Question:**

Four types of local anesthetic have been reported as possibly causing methemoglobinemia: prilocaine, benzocaine, lidocaine, and tetracaine. The mechanism for methemoglobin formation associated with prilocaine appears to be well understood. A metabolite, ortho-toluidine, is responsible for hemoglobin oxidation in the case of prilocaine. For what sub-groups of patients should the administration of prilocaine be avoided?

**Answer:**

Prilocaine should not be used in infants less than 6-months-of-age (except for transcutaneous anesthesia), in pregnant women, patients receiving other oxidizing drugs and patients with glucose-6-phosphate dehydrogenase (G-6-PD) deficiency. (Guay J. Methemoglobinemia related to local anesthetics: A summary of 242 episodes. 2009 Anesth Analg 108(3):837-845)

**Friday, May 28, 2010****Question:**

What is Jamaican vomiting sickness?

**Answer:**

Jamaican vomiting sickness is a disorder that results from ingesting unripe ackee fruit. The clinical features of this disorder include acute onset of severe vomiting and hypoglycemia, followed by convulsions and coma. Some cases also involve hypothermia. Some cases have been fatal. Symptoms of ackee poisoning typically occur 6-8 hours after ingestion, but can begin as early as 2 hours after ingestion. According to the cited reference, malnutrition may be associated with susceptibility to, and severity of, Jamaican vomiting sickness, especially among children. (Joskow R, et al. Ackee fruit poisoning: An outbreak investigation in Haiti 2000-2001 and review of the literature. 2006 Clin Tox, 44:267-273)

**Thursday, May 27, 2010****Question:**

What is the typical clinical pattern associated with tick paralysis and what entity is often confused with tick paralysis?

**Answer:**

Tick paralysis is typically described as an ascending paralysis with sensory sparing. It is caused by neurotoxic substances secreted by gravid ticks in the process of ingesting a blood meal. Tick paralysis is often mistaken for Guillain-Barre syndrome. (Diaz JH. A 60 year meta-analysis of tick paralysis in the United States: A predictable, preventable and often misdiagnosed poisoning. 2010 J Med Tox 6:15-21)

**Wednesday, May 26, 2010**

**Question:**

Under certain circumstances, the chemical glutaraldehyde may cause irritant symptoms as well as respiratory and/or skin sensitization and asthma. What is glutaraldehyde normally used for in the health care setting?

**Answer:**

Glutaraldehyde is used as an immersion chemical in disinfecting heat sensitive medical equipment such as endoscopes. (MMWR, May 14, 2010, 59(18):551-560)

**Tuesday, May 25, 2010****Question:**

Infection with Shiga toxin producing E. coli 0157 (STEC 0157) has been linked to consumption of what food? What preventive measures are recommended against this toxin induced disorder?

**Answer:**

Infection with Shiga toxin producing E. coli 0157 (STEC 0157) has been linked to consumption of undercooked beef. CDC recommends thorough hand washing after handling of raw beef, washing any surfaces that have come into contact with raw beef with hot soapy water, keeping beef separate from other food products and cooking ground beef to 160 degrees Fahrenheit (71.1 degrees C) as measured by a food thermometer. (MMWR, May 14, 2010, 59(18): 557-560)

**Monday, May 24, 2010****Question:**

Paraphenylenediamine (PPD) is an aromatic amine derived from paranitroaniline widely used as a hair dye ingredient. In Middle Eastern and Central Asian cultures it is often mixed with Henna (leaves of Lawsonia alba) and applied to color palms of hands and soles of feet and to dye hair a dark red shade. What are the characteristic clinical findings associated with suicidal ingestion of materials containing PPD? What are the alternate names used to designate PPD?

**Answer:**

A large percentage of cases involving intentional ingestion of PPD containing material present with upper airway edema. In addition, rhabdomyolysis with severe hyperkalemia and renal failure were reported in virtually all cases reported in the cited article. Alternate chemical names for PPD include PARA, 1,4- phenylenediamine, 6PPD, black for fur D, P- aminoaniline, phenylenediamine, p-benzenediamine, p-diaminobenzene. 1,4-diaminobenzene, oxidation base 10, C.I. 76060, developer PF, and zoba black. (Shalaby SA et al. Clinical profile of acute paraphenylenediamine intoxication in Egypt. 2010 Toxicology and Industrial Health 26(2):81-87)

**Friday, May 21, 2010****Question:**

Reactive airways dysfunction syndrome (RADS) is a somewhat controversial syndrome involving bronchial hyper-responsiveness following exposure to very high concentrations of gases, smoke, vapor or fumes with irritant properties. What chemical toxicants are most frequently implicated in the causation of RADS?

**Answer:**

The chemical toxicants most frequently implicated in the causation of RADS are as follows: toluene diisocyanate, chlorine, phosgene, sulfuric acid, fire smoke, phosphoric acid, hydrochloric acid, hydrogen sulfide, metam sodium and anhydrous ammonia. (Bardana E. Reactive airways dysfunction syndrome (RADS): guidelines for diagnosis and treatment and insight into likely prognosis. 1999 Ann Allergy Asthma Immunol, 83:583-586)

**Thursday, May 20, 2010****Question:**

Regular consumption of fish oils appears to reduce the risk for coronary artery disease. Large carnivorous fish such as swordfish and shark have high concentrations of mercury (> 1 microgram/gram) and tuna, pike, trout and bass have intermediate concentrations of mercury (0.1-0.5 micrograms/gram). Do over-the-counter fish oil preparations contain dangerous levels of mercury?

**Answer:**

The study cited below looked at five (5) different brands of over-the-counter fish oil and reported mercury levels that ranged from non-detectable to 10-12 micrograms/ liter. Thus, some brands of over the counter fish oil products may indeed contain small amounts of mercury. However, the amounts of mercury reported in this study are similar to those normally found in the serum of human subjects who consume regular amounts of fish and at recommended doses are presumably harmless to humans. (Foran SE, et al. Measurement of mercury levels in concentrated over-the-counter fish oil preparations. 2003 Arch Pathol Lab Med, 127:1603-1605)

**Wednesday, May 19, 2010****Question:**

The concurrent use of a CYP2D6 inhibitor with the drug tramadol may: 1- Increase serum levels of tramadol 2- Decrease serum levels of its active metabolite 3- Decrease the analgesic effect 4- all of the above

**Answer:**

Answer: All of the above (2010, The Medical Letter, 52(1338):40)

**Tuesday, May 18, 2010****Question:**

Bok choy (Brassica rapa chinensis), also known as Chinese white cabbage, contains a group of compounds known as glucosinolates. The breakdown products of glucosinolates have been implicated in the development of what endocrine disorder?

**Answer:**

Some of the breakdown products of glucosinolates (e.g. thiocyanates, nitriles, and oxazolidines) have been identified as having inhibitory effects on the thyroid. This has resulted, in some cases, in the development of severe hypothyroidism with myxedema coma. (Chu M and Seltzer TF. Myxedema coma induced by ingestion of raw bok choy. 2010 NEJM, 362:20:1945-1946)

**Monday, May 17, 2010****Question:**

In honor of the recent 2010 EAPCCT Congress held in Bordeaux, France.....what is the so-called "Bordeaux mixture"?

**Answer:**

"Bordeaux Mixture" is a copper-based fungicide consisting of CuSO<sub>4</sub> + Ca(OH)<sub>2</sub>. This mixture has been extensively used in Europe since the end of the 19th century to control vine (Vitis vinifera L.) fungal diseases, such as downy mildew caused by Plasmopara viticola. Other copper containing compounds have also been introduced including Cu-oxychloride 3Cu(OH)2-CuCl<sub>2</sub>, CuSO<sub>4</sub>·3Cu(OH)<sub>2</sub>, Cu<sub>2</sub>O, Cu(OH)<sub>2</sub>. Their long-term application and subsequent wash-off from treated plants has reportedly resulted in extensive Cu accumulation in some vineyard soils. (Komarek M, et al. Contamination of vineyard soils with fungicides: A review of environmental and toxicological aspects. 2010 Env Int'l, 36:138-151)

**Friday, May 14, 2010****Question:**

Radon-222 is a ubiquitous radioactive gas. It is present in the earth's crust and emanates from soils and rocks. Radon emits alpha particles that may damage lung tissues following inhalation. Radon-222 represents, with its progeny, one of the main sources of exposure to radioactivity in humans. What factors determine the concentration of radon inside of any given residential dwelling?

**Answer:**

The factors that determine the concentration of radon inside of any given building include the concentration of radon in the soil; the permeability of the ground; and the construction, building materials, and ventilation of the house. (Pavia M, et al. Meta-analysis of residential exposure to radon gas and lung cancer. 2003 Bull of the World Health Organization, 81:732-738)

**Thursday, May 13, 2010****Question:**

What is a complete carcinogen? What exposure is a complete carcinogen with regard to the development of skin cancer?



**Answer:**  
Ultraviolet radiation is a complete carcinogen with regard to the development of skin cancer. This means that on its own it has the ability to cause skin cancer without the need for other factors. However, in some cases, other co-carcinogens may have an expediting effect on skin cancers leading to earlier onset and or likelihood of numerous skin cancers. This fact does not impact the fact that UV radiation can induce skin cancer independently of other factors.(Murphy GM. Ultraviolet radiation and immunosuppression. 2009 Br J Derm,161(3):90-95)

**Wednesday, May 12, 2010**

**Question:**  
Clinical toxicologists are often called upon to evaluate situations involving possible exposure to indoor mold. Sometimes these analyses include the need for interpretation of a variety of attempts to quantify the number of mold spores or other mold products and to determine if specific levels of mold are associated with specific human health hazards. What is the relationship between these sorts of parameters and human health hazards?

**Answer:**  
The cited article notes Dose-response relationships between exposure to fungi (or fungal components) and symptoms are lacking. Credible studies that propose baseline levels for airborne fungal spores in buildings are limited and are nonexistent for the relevant metabolites (i.e., allergens, proteases, or glucans). Although a number of numeric standards for indoor fungi have been proposed, none are currently accepted by the scientific community. (Horner WE, et al. Guide for interpreting reports from inspections/investigations of indoor mold. 2008 J Allergy Clin Immunol, 121:592-7.)

**Tuesday, May 11, 2010**

**Question:**  
Severe envenomation following scorpion sting is reportedly more common in pediatric patients. What is the typical clinical syndrome associated with severe scorpion envenomation in children?

**Answer:**  
The clinical syndrome includes un-coordinated neuromotor hyperactivity, oculomotor and visual abnormalities, and respiratory compromise due to excessive respiratory tract secretions, airway obstruction, aberrant ventilatory effort, and occasional noncardiogenic pulmonary edema. The clinical pattern is a consequence of specific ion-channel toxins in the scorpion venom, which stimulate or potentiate action potentials throughout the peripheral nervous system. (Boyer LV, et al. Antivenom for critically ill children with neurotoxicity from scorpion stings. 2009 NEJM, 360:2090-2098)

**Monday, May 10, 2010**

**Question:**  
Fluoroquinolone (FQ) related tendinopathy has been most commonly described after the administration of ciprofloxacin. Other FQs such as norfloxacin, pefloxacin, ofloxacin and levofloxacin have also been reported to cause this problem. Which tendon is most commonly affected by FQ tendinopathy?

**Answer:**  
More than 95% of cases of tendinitis and rupture secondary to FQ involve the Achilles tendon. Other tendons that have been reported to be so affected include the quadriceps, peroneus brevis and the rotator cuff tendons. (Akali AU and Niranjana NS Management of bilateral Achilles tendon rupture associated with ciprofloxacin: A review and case presentation. 2008 J Plastic, Reconstr Aesthetic Surg, 61:830-834.)

**Friday, May 7, 2010**

**Question:**  
In 1997, a 48 year old chemistry professor died following an accidental skin exposure to a mercury containing compound. This individual spilled several drops of this mercury containing compound on her gloved hand. The absorption of this compound resulted in delayed cerebellar disease and death. What compound was this individual exposed to?

**Answer:**  
Dimethylmercury. This compound is lethal at a dose of approximately 400 mg of mercury (equivalent to a few drops, or about 5 mg per kilogram of body weight). (Delayed cerebellar disease and death after accidental exposure to dimethylmercury David W Nierenberg, Richard E Nordgren, Morris B Chang, Richard W Siegler, et al. The New England Journal of Medicine. Boston: Jun 4, 1998. Vol. 338, Iss. 23; pg. 1672, )

**Thursday, May 6, 2010**

**Question:**  
The FDA has recently required the manufacturer of clopidogrel (Plavix) to include a "boxed warning" regarding a subset of patients who may experience a less than optimal response to this anti-platelet drug. What is the basis for this possible poor response in some patients?

**Answer:**  
Genetic polymorphisms of the cytochrome P450 enzyme CYP2C19 are reported in some individuals. Clopidogrel is actually a prodrug and CYP2C19 is primarily responsible for the bioactivation of this drug. At least one genetic polymorphism associated with poor response to clopidogrel has been reported to occur in 15% of Caucasians, 17% of African Americans and 30% of Asians. (The Medical Letter, May 3, 2010, 52(1337):33)

**Wednesday, May 5, 2010**

**Question:**  
What is the half-life of lead in skeletal bone associated with prolonged occupational type exposures?

**Answer:**  
The skeletal half-life for lead in bone associated with prolonged occupational exposures ranges from 5-19 years. (Rabinowitz MB. Toxicokinetics of bone lead. 1991 Env Health Perspectives, 91:33-37)

**Tuesday, May 4, 2010**

**Question:**  
It is estimated that as many as 500 million people live near the world's 600 active volcanoes. These volcanoes degass a variety of pollutants during eruption. What are the pollutants of concern with regard to human health that may be degassed from active volcanoes?

**Answer:**  
The pollutants of concern include sulfur dioxide, carbon dioxide, radon and/or hydrogen sulphide. (Longo BM, et al. Cardiorespiratory health effects associated with sulphurous volcanic air pollution. 2008 Public Health, 122:809-820)

**Monday, May 3, 2010**

**Question:**  
What is argyria? What is the mechanism for this disorder and what is the currently recommended treatment?

**Answer:**  
Argyria is a slate blue or slate grey skin discoloration due to the ingestion or injection of silver. The mechanism causing argyria has not been fully elucidated. It is thought that silver may stimulate melanocytes to produce excess melanin. The cited article posits "the colorless silver in the dermis becomes brown-black in a reduction reaction when exposed to sunlight, similar to a reaction when light hits a silver grain on photographic paper". Avoidance of sun and sunscreens may decrease further skin discoloration. Currently, there is no effective treatment for argyria. (Chang AL, et al. A case of argyria after colloidal silver ingestion. J Cutan Pathol 2006; 33: 809-811.)

**Friday, April 30, 2010**

**Question:**  
With regard to "medical marijuana", most states limit the amount of marijuana that patients or patient caregivers can legally possess or grow. What is the range of these amounts and what is the general basis for determining these amounts?

**Answer:**  
The quantity of marijuana allowed to be held by patients with specific medical problems ranges from as little as 1 ounce or 6 plants (Alaska) to 24 ounces or 15 plants (Washington state). The determination of the allowable quantity appears to be arbitrary with Washington state applying a rule that the acceptable amount is what that state considers to be a "60-day supply". (Hoffman DE and Weber E. Medical marijuana and the law. 2010 NEJM, 362(16):1453-1457)



#### Thursday, April 29, 2010

##### Question:

Since December, 2009, 31 cases of anthrax infection in heroin users have been confirmed. All injection routes have been implicated in these cases but smoking and snorting have also been suggested as possible routes for infection. What was the clinical presentation for anthrax infection in these drug users?

##### Answer:

These cases did not present with typical anthrax (cutaneous, GI, or inhalational). Rather, a new presentation was documented and termed injectional. The presentations varied and included very vague prodromal symptoms. In some cases excessive bruising was present at drug injection sites. These patients appeared to be very ill and were normotensive with tachycardia. Most early findings were noted to be non-specific. In many cases the illness was noted to be biphasic with initial recovery followed by clinical deterioration within 72 hours. This decline led to rapid multisystem failure and shock. (Booth MG, et al. Anthrax infection in drug users. 2010 The Lancet, 375(9723): 1345-1346)

#### Wednesday, April 28, 2010

##### Question:

Gold mining and smelting using small-scale techniques is practiced in various communities in over 50 countries around the world. What heavy metal exposure may occur to those practicing small scale gold mining/smelting and how does that exposure take place?

##### Answer:

The potential exposure is to mercury vapor when mercury is used as an extraction adjunct for ore that may contain gold. Ore containing gold is first ground into a sludge. Liquid mercury is added to this mass and a small amount of amalgam, containing approximately 25% gold and 75% mercury is formed. The amalgam is then heated either by laying it on open charcoal fires or by applying a blow torch to it. Mercury evaporates at about 500 degrees Centigrade and gold is the remaining product. Exposure may occur by inhalation of this mercury vapor. As no sophisticated technology for this procedure is required, it is estimated that as many as 50 million people around the world may use mercury for small scale gold extraction in this way.(Bose-OREilly S, et al. Mercury as a serious health hazard for children in gold mining areas. 2008 Env Res, 107:89-97).

#### Tuesday, April 27, 2010

##### Question:

Individuals who donate platelets do so by undergoing a process known as apheresis. Occasionally apheresis patients develop severe hypocalcemia while undergoing the apheresis procedure. What is the mechanism for the development of severe hypocalcemia related to apheresis?

##### Answer:

Severe hypocalcemia has been reported in some individuals undergoing apheresis due to calcium chelation by the sodium citrate anticoagulant that is often used during the apheresis process. (Bell AM, et al. Severe citrate toxicity complicating volunteer apheresis platelet donation. 2007 J Clin Apheresis, 22:15-16)

#### Monday, April 26, 2010

##### Question:

What is iqmik?

##### Answer:

Iqmik is a smokeless tobacco product that is popular among some native Alaskans. Iqmik is produced by chewing tobacco leaf together with punk ash (ashes from the burning of *Phellinus igniarius* fungus) or Alaska willow (*Salix alaxensis*). The ash component of iqmik renders the saliva alkaline and thus results in a significant increase in the absorption of nicotine. (Pappas RS, et al. Analysis of toxic metals in commercial moist snuff and Alaskan iqmik. 2008 J Analytical Tox, 32 (4):281-291.)

#### Friday, April 23, 2010

##### Question:

While amiodarone is generally well tolerated by most patients, hepatotoxicity and neurotoxicity due to this drug has reportedly developed in some rare cases. What is the mechanism for the hepatotoxicity caused by amiodarone? What is the mechanism for the neurotoxicity caused by amiodarone?

##### Answer:

Hepatotoxicity related to amiodarone is theorized to be due to the development of hepatic steatosis caused by inhibition of mitochondrial beta-oxidation of short, medium and long-chain fatty acids. The mechanism causing neurotoxicity is unclear but intracellular inclusion bodies have been reported and may play a role in demyelination of peripheral nerves. (Arkun A, et al. Hepatic dysfunction and neurotoxicity in a patient receiving long-term low dose amiodarone therapy. 2010 J Emerg Med, 38(3):337-339)

#### Thursday, April 22, 2010

##### Question:

Individuals suffering from hyponatremia may develop what life threatening problem if low serum sodium is corrected too rapidly?

##### Answer:

Extra pontine myelinolysis and/or central pontine myelinolysis may result in cases where hyponatremia is corrected too rapidly. (Morita S, et al. Risk factors for rhabdomyolysis in self induced water intoxication (SIWI) patients. 2010 J Emerg Med, 38(3):293-296)

#### Wednesday, April 21, 2010

##### Question:

What is the mechanism of toxicity associated with exposure to environments containing elevated concentrations of carbon dioxide (CO2)?

##### Answer:

The mechanism for toxicity associated with exposure to environments containing elevated concentrations of carbon dioxide generally is considered to be primarily due to asphyxia secondary to the creation of oxygen poor breathable air caused by the displacement of oxygen by CO2. However, other, yet to be defined mechanisms, involving direct organ toxicity may also be at play. The cited article notes "Elevated atmospheric CO2 has been shown to produce direct toxicity independent of associated hypoxia." (Dunford JV, et al, Asphyxiation due to dry ice in a walk in freezer. 2009 J Emerg Med, 34 (4): 353-356)

#### Tuesday, April 20, 2010

##### Question:

A high frequency of long QT syndrome associated with methadone therapy has been reported from a variety of sources. What factors contribute to the development of long QT syndrome in the population of individuals taking methadone?

##### Answer:

Methadone dose, use of CYP3A4 inhibitors, low potassium level, and hepatic dysfunction all contribute to the drug induced long QT syndrome associated with methadone.(Ehret GB, et al. Drug induced long QT syndrome in injection drug users receiving methadone.2006 Arch Int Med; 166(12):1280-1287.)

#### Monday, April 19, 2010

##### Question:

Sudden sensori-neural hearing loss is defined as hearing loss of at least 30 dB in three sequential frequencies in the standard pure-tone audiogram over three days or less. What drugs and drug classes have been associated with sudden sensorineural hearing loss?

##### Answer:

The following drugs have been reported to cause sudden sensorineural hearing loss: penicillin, estrogens, phosphodiesterase inhibitors, pegylated interferon with ribavirin, aminoglycosides, some chemotherapy agents and intravenous cocaine. (Schreiber BE, et al. Sudden sensorineural hearing loss. 2010 The Lancet; 375:1203-1211)

#### Friday, April 16, 2010

##### Question:

Dialysis Disequilibrium Syndrome (DDS) is characterized by neurological symptoms in some patients undergoing hemodialysis. What are the toxicologic causes for DDS?

**Answer:**

DDS is NOT caused by any toxins or toxicant! Dialysis Disequilibrium Syndrome is characterized by neurological symptoms associated with the rapid removal of urea during hemodialysis. Due to rapid hemodialysis, an osmotic gradient develops between the brain and the plasma. Cerebral edema results and may manifest as a variety of neurological symptoms including headache, nausea, vomiting, muscle cramps, tremors, altered level of consciousness, and seizures. Death can result from severe cerebral edema. Recent reports suggest the role of urea dis-equilibrium (with a smaller contribution from organic osmolytes) as the pathophysiological mechanism responsible for this syndrome. (Patel N, et al. Dialysis disequilibrium syndrome: A narrative review. 2008 Seminars in Dialysis, 21(5): 493-498)

**Thursday, April 15, 2010****Question:**

What is the typical course for respiratory impairment that develops secondary to smoke inhalation in firefighters?

**Answer:**

Smoke inhalation during firefighting causes relatively mild and reversible respiratory impairment. (Aldrich TK, et al. Lung function in rescue workers at the World Trade Center after 7 years. 2010 NEJM; 361(14):1263-1272)

**Wednesday, April 14, 2010****Question:**

What is bromadiolone, what is the mechanism for its toxicity in humans and what is the recommended treatment for toxicity due to this agent?

**Answer:**

Bromadiolone is a superwarfarin rodenticide. It is a vitamin K antagonist and inhibits hepatic synthesis of coagulation factors II, VII, IX, X as well as proteins S and C. Treatment for significant toxicity from this chemical involves careful clinical monitoring as well as the judicious administration of vitamin K1 (Lo, et al. Bromadiolone toxicokinetics: Diagnosis and treatment implications. 2008, Clin Tox,46:703-710)

**Tuesday, April 13, 2010****Question:**

Hydrogen peroxide is an oxidizing agent found in many different settings both domestic and industrial. What are the most commonly seen concentrations of hydrogen peroxide and what are the various concentrations of this chemical used for?

**Answer:**

Topical disinfectants usually contain either 3% or 6% hydrogen peroxide. Concentrations of 33 % or 35% hydrogen peroxide are often used as bleaching agents. Extremely high concentrations of this chemical (80%-90%) are sometimes used in combination with other substances to fuel rocket engines. (Rider SP, et al. Cerebral air gas embolism from concentrated hydrogen peroxide ingestion. 2008, Clin Tox 46:815-818)

**Monday, April 12, 2010****Question:**

What are the classic manifestations of vitamin A toxicity?

**Answer:**

LIVER: hepatosplenomegaly, elevated liver tests, ascites, portal hypertension, cirrhosis; CNS: increased intracranial pressure, headache, vertigo, diplopia, ataxia, coma; INTEGUMENT: thinning of eyebrows, dry mucous membranes, angular cheilitis, gingivitis desquamation, erythema, pruritus; MUSCULOSKELETAL: bone pain, cortical thickening of long bones, soft tissue calcification, muscle pain (Miksad R, et al. Hepatic hydrothorax associated with vitamin A toxicity. 2002, J Clin Gastroent, 34(3):275-279)

**Friday, April 9, 2010****Question:**

Will commonly employed urine immunoassays for amphetamines also detect MDMA?

**Answer:**

The commonly employed monoclonal amphetamine and methamphetamine immunoassays are capable of detecting MDMA as a result of cross-reactivity. However, the sensitivity of these tests with regard to MDMA is roughly 50% less than for methamphetamine or amphetamine. Consequently, very high urine concentrations of MDMA must be present for amphetamine immunoassays to detect MDMA. (Moeller KE, et al. Urine drug screening: Practical guide for clinicians. 2008, Mayo Clin Proc 83(1):66-76)

**Thursday, April 8, 2010****Question:**

For roughly the past 15 years it has been recognized that an important drug-food interaction occurs between grapefruit/grapefruit juice and various drugs including calcium channel blockers, lipid lowering agents, cyclosporin, certain antibiotics (as well as other drugs) resulting in elevated blood levels and potential toxicity. What is the mechanism for this food-drug interaction?

**Answer:**

The primary mechanism involves a decrease in the metabolism ("first pass") of certain drugs due to inhibition of intestinal CYP3A4. Grapefruit juice also inhibits intestinal P-glycoprotein-mediated efflux transport of certain drugs thereby increasing their bioavailability. In addition, grapefruit juice (and other fruit juices as well) may influence a variety of other influx transporters known as organic anion transporter polypeptides (OATPs). (Mertens-Talcott SU, et al. Grapefruit-drug interactions: Can interactions with drugs be avoided? 2006, J Clin Pharm, 46:1390-1416.

**Wednesday, April 7, 2010****Question:**

What are the proposed mechanistic differences between solvent induced hearing loss and noise exposure related hearing loss?

**Answer:**

Solvents, at appropriate exposure levels and doses, are theorized to affect both the hair cells and central auditory structures while noise exposure primarily affects the outer and inner hair cells of the cochlea. (Fuente A., et al Peripheral and central auditory dysfunction induced by occupational exposure to organic solvents. 2009, J Occ Env Med, 51(10):1202-1211)

**Tuesday, April 6, 2010****Question:**

Which valence state of chromium is generally considered to be carcinogenic?

**Answer:**

Since the early 1980s both the International Agency for Research on Cancer (IARC) and the National Toxicology Program of the United States (NTP) have categorized chromium as a human carcinogen. This is based on epidemiologic evidence that hexavalent chromium (chrome in valence state six (Cr6)) at medically important exposures and in medically important doses, may cause cancers of the lung, the nose, and the nasal sinuses. It is generally accepted that only Cr6 is carcinogenic. There is good evidence that chrome in valence state three is not a human carcinogen. (Cole P, Rodu B. Epidemiologic studies of chrome and cancer mortality: A series of meta-analyses. 2005, Reg Tox & Pharm, 43:225-231)

**Monday, April 5, 2010****Question:**

In September of 1987, a radiological exposure incident occurred in central Brazil. This incident resulted in contamination of 249 individuals and required contamination checks for more than 125,000 inhabitants of the area. What city in Brazil was the site of this incident, what was the basis for the radiological release and what radiologic isotope was involved?

**Answer:**

The isotope involved was cesium 137 and the city was Goiânia, Brazil. The Instituto Goiano de Radioterapia in Goiânia, moved to new quarters and in the move abandoned a teletherapy unit containing a cesium source [137Cs; activity: 50.9 TBq]. Several scavengers found this teletherapy unit and dismantled it. Subsequently the cesium source was widely disseminated as follows: "After several days they managed to break open the stainless steel cylinder with a sledgehammer and discovered a platinum capsule, which was the housing for the cesium source (100 g soluble (CsCl<sub>2</sub>). This capsule was opened with a saw and the powder (referred to by witnesses as carnival glitter) discovered. The whole lot was purchased by a waste paper dealer, attracted to the bluish light emitted by the material in the dark. Subsequently, he cut the platinum cylinder into altogether seven large and over fifty smaller pieces (some of which were the size of rice grains), which were distributed among relatives and friends. The radioactive material was further distributed by children playing in the scrap paper storage area and by workers who took some of the radioactive material home. Thereby, the cesium was spread onto paper, clothing, floors, walls, and was even consumed through contaminated food. Within a few days exposed individuals fell ill and sought medical care, and contaminated three medical practices and five hospitals."(Steinhausler F. Chernobyl and Goiânia lessons for responding to radiological terrorism. 2005, Health Physics, 89(5):566-574)

**Friday, April 2, 2010****Question:**

What form of leukemia may be treated using the arsenic containing medication known as Trisenox and what form of arsenic is contained in that drug preparation?

**Answer:**

Arsenic trioxide (As<sub>2</sub>O<sub>3</sub>), has important anti- tumor properties. This agent is a potent inducer of antileukemic responses, and it is now approved by the Food and Drug Administration for the treatment of acute promyelocytic leukemia in humans under the trade name Trisenox.(Platanias LC. Biological responses to arsenic compounds.2009, J Biol Chem, 284:18583-18587).

**Thursday, April 1, 2010****Question:**

Acrolein is a reactive aldehyde often used as an intermediate in chemical manufacturing and as a biocide. Which individuals are most at risk for receiving exposures to acrolein (that may or may not be medically important)?

**Answer:**

While small amounts of acrolein are formed naturally in the human body, those Individuals likely to receive the highest exogenous exposures include smokers, those inhaling second-hand smoke and persons (without adequate protective equipment) in close proximity to wood and/or plastic smoke. No significant acrolein exposure is expected from ingestion of drinking water or from dermal contact during bathing or showering. (Faroon O., et al. Acrolein health effects. 2008, Toxicol Ind Health, 24:447-490).

**Wednesday, March 31, 2010****Question:**

What is "hard metal" and what is "hard metal disease"?

**Answer:**

"Hard metals" are materials in which metallic carbides are bound together by a soft and ductile metal binder, usually cobalt or nickel. The term cemented carbide is widely used in the USA, but these materials are better known world-wide as hard metals. Hard metals are manufactured by a powder metallurgy process consisting of a sequence of controlled steps designed to obtain a final product with specific properties, microstructure and performance. Hard metal disease is a rare occupational lung disease, a fibrosing alveolitis, caused by metallic cobalt-containing particles. (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, 2006, vol. 86. Cobalt in hard metals and cobalt sulfate, gallium arsenide, indium phosphide and vanadium pentoxide. accessed at <http://monographs.iarc.fr>)

**Tuesday, March 30, 2010****Question:**

Sulfur mustard is a strong alkylating agent able to react with all dermal constituents. What are the three major dermal pathologic findings associated with exposure to sulfur mustard and what is the critical subcellular lesion associated with exposure to this agent?

**Answer:**

The development of erythema, blisters and ulcers are the three major pathologic skin findings. Typical erythema and skin edema formation occurs several hours following skin contact, which is followed by subepidermal blister formation. Erythema can occur 48h after sulfur mustard exposure at a threshold dose while blister formation occurs at higher doses. The blisters are characterized by small vesicles, which coalesce at a later point in time to form large blisters or bullae. Exposure to higher concentrations of SM results in ulcers penetrating dermal structures of the skin. DNA damage is the critical lesion. (Kehe K, et al. Molecular toxicology of sulfur mustard-induced cutaneous inflammation and blistering. 2009, Toxicology, 263:12-19)

**Monday, March 29, 2010****Question:**

The internet is replete with websites that indicate taking amoxicillin can result in a false positive urine screen for cocaine metabolites. What is the evidence that amoxicillin is capable of causing this false positive result?

**Answer:**

There really is no scientific evidence. One article (referenced below) reviewed the medical literature and found no experimental evidence to support this notion. In addition, they administered amoxicillin to 33 test subjects and found 31 produced urine negative for cocaine metabolites. Two specimens were positive but those specimens proved to reflect actual cocaine use as confirmed using GC/MS. These authors concluded that "amoxicillin is unlikely to produce false positive urine screens for cocaine metabolites." (Reisfield GM, et al. Failure of amoxicillin to produce false-positive urine screens for cocaine metabolites. 2008, J Analytical Tox, 32:315-318.)

**Friday, March 26, 2010****Question:**

Trichloroethylene (TCE) has been widely used as an industrial solvent over the past several decades. What are the main occupations and industries where TCE may have been (or may be) used?

**Answer:**

The main industries are those involved with metal degreasing and aircraft/aerospace maintenance or other metal manufacturing work. Other industries include the iron/steel industries, where TCE may have been used as a general solvent and degreaser; painting, where products may have been cleaned with TCE or TCE was used as a solvent in the paint; the electronics industry, where TCE was used as a degreaser; the chemical industry, where TCE was used in the production of various products; the printing industry, where TCE may have been used to clean machinery and as a solvent in dyes; shoe manufacturing, where TCE was used as a solvent in the glues; and jewellery manufacturing, where TCE may have been used as a general solvent. (Mandel JH, et al. Occupational trichloroethylene exposure and non-Hodgkin's lymphoma: a meta-analysis and review. 2006, Occup Environ Med, 63:597607)

**Thursday, March 25, 2010****Question:**

What are the pulmonary effects that may result from the aspiration of commercially available lamp oil (paraffin)

**Answer:**

Pulmonary aspiration of lamp oil may cause lipoid pneumonia and/or severe chemical pneumonitis. The severity of the clinical manifestations is undoubtedly related to the amount of lamp oil aspirated. (Yu M, et al. Multiple organ failure following lamp oil aspiration. 2007, Clin Tox, 45:304-306)

**Wednesday, March 24, 2010****Question:**

Benzene, at medically important exposure levels and medically important absorbed doses, has been associated with the development of acute myelogenous leukemia (AML). What is the association between benzene exposure and chronic myelogenous leukemia (CML)?

**Answer:**

Numerous reviews based on case series and cohort studies have not shown an association. A recent meta-analysis addressed the association between benzene exposure and CML. Six case-control studies were identified derived from occupational groups, cancer registries, and a clinical laboratory. Their exposure ascertainment are all based on job histories, job-exposure matrices, or industrial hygiene data. The odds ratios (ORs) for individual studies ranged from 0.73 to 1.2. The pooled OR was 1.003 with 95% confidence interval (CI) of 0.941.07 (p = 0.98) for both a fixed effects model and a random effects model. The meta-analysis report concluded the case-control literature indicates that chronic myelogenous leukemia does not appear to be related to benzene exposure. (Lamm SH, et al. Chronic myelogenous leukemia and benzene exposure: A systematic review and meta-analysis of the case control literature. 2009, Chemico-Biological Interactions, 182:93-97.)

**Tuesday, March 23, 2010**

**Question:**

Risk assessment methodologies often consider the ingestion of soil as an important potential route for toxicant exposure in children. How much soil are children thought to ingest on a daily basis?

**Answer:**

Several soil ingestion studies have reported that some children may ingest substantial amounts of soil however EPA estimates relatively small amounts of daily soil ingestion for children (< 100 mg/day) with the upper 95th percentile being estimated to ingest an average of 200 mg of soil per day. (Calabrese EJ et al. Soil ingestion: A concern for acute toxicity in children. 1997, Env Health Perspectives 105:1354-1358). A more recent report indicates children's mean soil ingestion rates ranged from 37 to 207 mg/day depending on the tracer, with the highest values based on titanium as a tracer. Adult mean soil ingestion rates ranged from 23 to 625 mg/day depending on the tracer, with the highest value based on titanium as a tracer. Soil ingestion rate estimates were more variable in adults than in children. (David S, Mirick DK. Soil ingestion in children and adults in the same family. 2006, J Exp Sci and Env Epi, 16:63-75.)

**Monday, March 22, 2010**

**Question:**

What are the acknowledged predictors of INH-associated liver injury?

**Answer:**

Predictors of INH-associated liver injury include pre-existing liver disease, HIV infection, injection drug use, concurrent alcohol consumption, pregnancy or the immediate post-partum period (

**Friday, March 19, 2010**

**Question:**

What is western red cedar asthma (WRCA) and what is the chemical contained in this wood recognized as the putative toxicant associated with the development of this disorder?

**Answer:**

WRCA was first described in 1969, as the development of irritant and respiratory symptoms that progresses to asthma as a result of machining western red cedar. WRCA was eventually further characterized (Chan-Yeung, M, et al. 2003, Am J Ind Med, 44:236-245) and plicatic acid was identified as the specific etiological agent involved. (Dimich-Ward H, et al. Quality of life and employment status of workers with western red cedar asthma. 2007, J Occup Env Med, 49:1040-1045)

**Thursday, March 18, 2010**

**Question:**

What is "black tar heroin" (BTH)?

**Answer:**

Black tar heroin is an unpurified derivative of the opium poppy, usually described as a firm, gummy, dark brown to black material. BTH is often smuggled from Mexico into the United States, where it is transported and distributed, typically in the Pacific Northwest where it is essentially the exclusive form of heroin encountered in the north west USA. (Dunbar NM, et al. Necrotizing fasciitis: manifestations, microbiology and connection with black tar heroin. 2007, J Forensic Sci, 52(4):-920-923)

**Wednesday, March 17, 2010**

**Question:**

What is the drug of choice to prevent ulcers in individuals taking non-steroidal anti-inflammatory drugs including aspirin?

**Answer:**

Proton-pump inhibitors (PPI's) (esomeprazole,lansoprazoleomeprazole,pantoprazole,rabeprazole) are capable of preventing aspirin or NSAID related ulcers as detected on endoscopy. The degree to which PPI's may prevent bleeding and/or clinical symptoms has yet to be determined. (The Medical Letter, 2010, 52(1333):17-19)

**Tuesday, March 16, 2010**

**Question:**

Emergency physicians and nurses often draw blood from patients in order to determine the blood ethanol concentration. When the skin is prepared by swabbing with isopropyl alcohol containing pads, what is the likelihood that the blood ETHANOL concentration will become falsely elevated due to the application of isopropyl alcohol to the skin?

**Answer:**

While some jurisdictions may actually require the use of "non-alcohol containing skin disinfectants" when preparing to draw blood for ethanol determinations, it is highly unlikely that the use of a prep pad containing isopropyl alcohol will cause a false elevation of blood ethanol levels. One study evaluating this question reported: "This study suggests that isopropyl skin prep pads do not cause significant false-positive blood ethanol levels. Thus, legal authorities and medical personnel should be aided in their interpretation of blood ethanol results, assured that the use of isopropyl skin prep pads are unlikely to be a contributing factor in the test results." (Miller MA, et al. Isopropyl alcohol pad use for blood ethanol sampling does not cause false positive results. 2007, J Emerg Med, 33(1):9-10)

**Monday, March 15, 2010**

**Question:**

Ambient particulate air pollutants include so-called coarse particles with aerodynamic diameter (AD) ranging from 2.5 to 10 microns (PM10), fine particles (AD 0.1 microns to 2.5 microns; PM 2.5), and ultrafine particles (UFPs) (AD less than 0.1 microns). These particulate air pollutants may be derived from both human activities and natural sources. Which specific particles are derived from which specific sources?

**Answer:**

PM10 particles related to human activities are derived from road and agricultural dust, tire wear emissions, wood combustion, construction and demolition works, and from some mining operations. Natural sources of PM10 include windblown dust and wildfires. Fine particles are thought to be primarily derived from gas to particle conversions and during fuel combustion and other industrial activities. Sources of PM2.5 may include some power plants, some oil refinery and metal processing facilities, tailpipe and brake emissions from mobile sources, residential fuel combustion, and wildfires. The primary contributors to UFPs are tailpipe emissions from mobile sources including some motor vehicles, aircraft, and marine vessels. (Simkhovich BZ, et al. Air pollution and cardiovascular injury: Epidemiology, toxicology and mechanisms, 2008, J Am Coll Cardiol., 52: 719-726)

**Friday, March 12, 2010**

**Question:**

The heavy metal cadmium (Cd) is associated with a number of industrial processes and may be absorbed from cigarette smoke, water, food and/or air contaminations. Cd is known to have the potential to exert adverse effects in both experimental animals and humans, targeting kidney, liver and the vascular system under specific circumstances. What mechanisms may explain much of Cd toxicity?

**Answer:**

The molecular mechanisms accounting for the biological effects of Cd are not well-understood and the toxicity targets have not yet been fully identified. However, recent work indicates that Cd may exert important effects on mitochondria by the induction of oxidative stress, modulation of intracellular redox homeostasis, and lipid peroxidation, mutating mitochondrial DNA, alteration of gene expression and ultimately inducing apoptosis. (Cannino G, et al. Cadmium and mitochondria. 2009, Mitochondrion, 9:377-384)

**Thursday, March 11, 2010**

**Question:**

What is cyclosarin?

**Answer:**

Cyclosarin is a member of the nerve agent family that was found after the first Gulf War (in 1991) to be incorporated in Iraqi chemical weapons stocks. It is a liquid substance with an aging half-life of 40 hours and it differs from sarin by having a bulky cyclohexyl group instead of an isopropyl group. It is this cyclohexyl group causing "steric hindrance" that is presumed to be the reason for the low potency of some AChE reactivators. (Kuca K, et al. Potency of five structurally different acetylcholinesterase reactivators to reactivate human brain cholinesterases inhibited by cyclosarin. 2007, Clin Tox, 45(5):512-515)

**Wednesday, March 10, 2010**

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**Question:**

Jimsonweed (*Datura stramonium*) is a plant from the nightshade family that contains anticholinergic alkaloids including atropine and scopolamine. This plant has been associated with the production of the anticholinergic toxidrome in persons ingesting parts of this plant or extracts of parts of this plant. What part of the jimsonweed plant contains the highest concentration of atropine alkaloids?

**Answer:**

The concentration of anticholinergics in this plant may vary over time and in differing parts of the plant but it is generally agreed that the seeds of the jimsonweed plant contain the highest concentration of anticholinergic alkaloids (approximately 0.1 mg of atropine per seed) (CDC MMWR, 2010, 59(4):102-104)

**Tuesday, March 9, 2010****Question:**

The ingestion of water containing inorganic arsenic is associated with the development of changes in pigmentation of the skin of the trunk and limbs, nodular keratosis of the plantar feet and the palms, and may be the first indicator of the diagnosis of arsenic toxicity. How long after initial exposure to arsenic do related skin lesions occur and are the skin lesions associated with relatively low or relatively high arsenic doses?

**Answer:**

According to a recent review, the majority of individuals confirmed to have arsenic related skin lesions had consumed water containing arsenic at concentrations higher than 200 mcg/L. In addition, this review indicated that the average latency for skin lesions was 23 years from first exposure. There is no rationale to expect skin lesions in people who ingest water containing lesser concentrations of arsenic for only short periods of time (Smith AH and Steinman CM. Health effects of arsenic and chromium in drinking water: Recent human findings. 2009, Ann Rev Pub Health, 30:107-122)

**Monday, March 8, 2010****Question:**

A number of important cardiovascular medications, including thiazide diuretics and beta-blockers, have been associated with an increased risk of developing diabetes. Statin drugs have recently been added to this list. What is the risk of developing diabetes in association with statin medications?

**Answer:**

A recent collaborative meta-analysis reported a small increased risk for the development of diabetes in those taking statin drugs. The identified risk was small, in the range of 9% (OR= 1.09) and was primarily noted for older individuals with no risk seen in patients younger than 60 years of age. (Sattar N, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomized stain trials. Lancet, 2010, 375(9716):735-742)

**Friday, March 5, 2010****Question:**

What are the IRREVERSIBLE adverse effects of the anti-seizure medication vigabatrin (Sabril)? Scroll down for the answer

**Answer:**

The irreversible adverse effects of vigabatrin are concentric visual field deficits associated with retinal dysfunction. It has been reported that after treatment with vigabatrin for longer than six months, these adverse effects occurred in 25% of patients 8-12 year of age and in 40% of those older than 12 years. (The Medical Letter, 2010, 52(1332):14-15)

**Thursday, March 4, 2010****Question:**

In 2004, the FDA and EPA revised their guidelines on fish consumption to minimize methylmercury exposure and recommended limiting intake to no more than 12 oz of fish per week. Recommendations also include avoiding fish that contain high levels of methylmercury. Which species of fish are specifically classified as containing "high levels of methylmercury"? Scroll down for the answer

**Answer:**

Fish that contain high levels of methylmercury include shark, swordfish, king mackerel, and tilefish. (Dovydaitis T. Fish consumption during pregnancy: An overview of the risks and benefits. J of Midwifery and Womens Health, 2008, 53(4):325-330)

**Wednesday, March 3, 2010****Question:**

Hypercalcemia often presents with relatively non-specific symptoms. What are the classic symptoms associated with hypercalcemia and how do these symptoms correlate with the clinical setting? Scroll down for the answer

**Answer:**

The classic symptoms usually associated with hypercalcemia are confusion, mental lethargy, anorexia, constipation, nausea, polyuria and polydipsia. The severity of these symptoms usually correlates with the severity of the hypercalcemia and the speed with which the hypercalcemic state develops. (Halldanarson TR et al. Oncologic emergencies: Diagnosis and treatment. 2006, Mayo Clinic Proceedings, 81(6):835-848)

**Tuesday, March 2, 2010****Question:**

In patients taking digoxin, macrolide antibiotics can cause digoxin toxicity. What is the mechanism of this drug interaction, and which macrolide imparts the greatest risk? Scroll down for the answer

**Answer:**

Digoxin is a substrate for the multidrug efflux pump P-glycoprotein (P-gp), which normally limits the intestinal absorption of digoxin and promotes renal digoxin elimination. Erythromycin, clarithromycin, and azithromycin all inhibit this pump and thereby increase the risk of digoxin toxicity. The risk is highest with clarithromycin, which is a more potent P-gp inhibitor than either erythromycin or azithromycin. Compared to the use of cefuroxime, erythromycin and azithromycin both increase the risk of digoxin toxicity roughly 3-fold, while clarithromycin increases it roughly 14-fold. (Gomes T, Mamdani MM, Juurlink DN. Macrolide-Induced Digoxin Toxicity: A Population-Based Study. Clinical Pharmacology and Therapeutics 2009;86(4):383-386)

**Monday, March 1, 2010****Question:**

What book, published in 1962, was among the political and social forces that led the Nixon administration in 1970 to establish the Environmental Protection Agency (EPA)? Scroll down for the answer

**Answer:**

The book was Silent Spring authored by Rachel Carson. (Murray RW. Forty years after Silent Spring. 2002, Analytical Chemistry, 74:501A)

**Friday, February 26, 2010****Question:**

What is the drug of choice for patients requiring parenteral treatment for malaria caused by *Plasmodium falciparum*? What is the availability of this agent and from what source is it pharmaceutically derived? Scroll down for the answer

**Answer:**

Artesunate is the drug of choice for patients requiring parenteral treatment for this form of malaria. It is derived from the herbal artemisinin. This agent is not marketed in the U.S. but is available from the Malaria Branch of the CDC (call 770-488-7788 or (after hours) 770-488-7100). Approximately 1,500 cases of malaria are diagnosed in the United States each year and approximately 10% of them are cases of severe malaria, with a significantly higher chance of death. (The Medical Letter, May 19, 2008, 50(1286) and [http://www.cdc.gov/malaria/diagnosis\\_treatment/artesunate.html](http://www.cdc.gov/malaria/diagnosis_treatment/artesunate.html))

**Thursday, February 25, 2010****Question:**

What are the currently recognized contraindications for the use of propofol? Scroll down for the answer

**Answer:**

Propofol is contraindicated in any patient with known or suspected allergy to propofol, eggs, or soy products. (Miner J and Burton JH. Clinical Practice Advisory: Emergency department procedural sedation with propofol. 2007, Ann Emerg Med 50:182-187)

#### Wednesday, February 24, 2010

**Question:**

Does radiation exposure due to diagnostic CT scanning increase cancer risk? Scroll down for the answer

**Answer:**

Evidence from epidemiologic studies indicates that organ doses associated with the common CT study (two or three scans, resulting in a dose in the range of 30 to 90 mSv) result in an increased risk of cancer. The evidence is reasonably convincing for adults and very convincing for children. (Brenner DJ and Hall EJ. Computed tomography- An increasing source of radiation exposure. 2007, NEJM 357:2277-2284.)

#### Friday, February 19, 2010

**Question:**

Diphenhydramine has recently been reported to cause opsoclonus, which refers to involuntary, nonrhythmic, darting oscillations (often with both vertical and horizontal components, sometimes seen sequentially and sometimes combined to form a looping motion) of the eyes. Besides diphenhydramine, what can cause opsoclonus?

**Answer:**

Opsoclonus is seen most commonly in viral or paraneoplastic encephalitis but has also been reported in patients exposed to lithium or to organophosphorous compounds. (Irioka T, et al. Opsoclonus caused by diphenhydramine self-poisoning. 2009, Journal of Neuro-Ophthalmology 29(1):72-73.) James M. Madsen, MD, MPH, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; zmaddoc@gmail.com

#### Thursday, February 18, 2010

**Question:**

Thallium is well known for causing alopecia. It can also result in painful neuropathies and in nail erosion. What skin changes may occur following exposure to thallium?

**Answer:**

A metallic discoloration of the skin has been reported to precede alopecia following thallium poisoning. (Aasly JO. Thallium intoxication with metallic skin discoloration. 2007, Neurology 68(21):1869.) James M. Madsen, MD, MPH, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; zmaddoc@gmail.com

#### Wednesday, February 17, 2010

**Question:**

Low-grade envenomations from the Arizona bark scorpion (*Centruroides sculpturatus*, also called *Centruroides exilicauda*) can cause local pain and paresthesias either at the site of the stings (Grade I envenomations) or remote from the sites of the stings (Grade II); high-grade envenomations can produce either neuromuscular effects (typically, uncontrollable writhing movements) or cranial-nerve abnormalities (Grade III); they may also result in both neuromuscular and cranial-nerve effects (Grade IV effects). What eye findings may be seen in Grade III or IV envenomations by *C. sculpturatus*?

**Answer:**

Opsoclonus (involuntary roving or darting eye movements) are often seen in *C. sculpturatus* patients. Suchard JR, Hilder R. Atropine use in *Centruroides* scorpion envenomation. 2001, Clinical Toxicology, 39(6):595-598.) James M. Madsen, MD, MPH, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; zmaddoc@gmail.com

#### Tuesday, February 16, 2010

**Question:**

The United States Food and Drug Administration (FDA) classifies drugs into four pregnancy categories depending upon the expected effects of these drugs on the fetus. Category X represents drugs clearly contraindicated in pregnancy. Name at least six Category X drugs.

**Answer:**

Category X drugs, which according to the FDA are clearly contraindicated in pregnancy, include danazol (an androgen), methotrexate (an antimetabolite), warfarin (a coumadin derivative), diethylstilbesterol (an estrogen), misoprostol, oral contraceptives, isotretinoin (a retinoid), radioactive iodine (sodium iodide-128), and thalidomide. (Buhimschi BS, Weiner CP. Medications in pregnancy and lactation. Part 1. Teratology. Obstet Gynecol 2009 Jan, 113(1):166-188.) James M. Madsen, MD, MPH, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; zmaddoc@gmail.com

#### Monday, February 15, 2010

**Question:**

Bidirectional ventricular tachycardia should raise suspicion for toxicity due to what drug?

**Answer:**

Bidirectional ventricular tachycardia should always raise suspicion for toxicity due to digitalis. (Goldberger AL, et al, Basic approach to arrhythmias due to digitalis toxicity. 2010, UpToDate, www.utd.com, version 17.3)

#### Friday, February 12, 2010

**Question:**

Aluminum phosphide is a pesticide used for the fumigation of a variety of agricultural products. On contact with moisture, this compound reacts with water to form phosphine gas. Phosphine gas (PH<sub>3</sub>) is said to have a "garlic or fishy odor" but the presence or absence of this odor may not be the best way to identify that a phosphine exposure has indeed occurred. What is the probable toxicological mechanism of action for this potentially lethal poison (i.e. phosphine gas)?

**Answer:**

The most likely mechanism for phosphine toxicity involves the inhibition of enzymes (including cytochrome c oxidase) resulting in the generation of superoxide radicals and cellular peroxides with subsequent lipid peroxidation. Other oxidant mechanisms may also be at play but lipid peroxidation is the most likely common mechanism for toxicity. (Sudakin DL. Occupational exposure to aluminum phosphide and phosphine gas? A suspected case report and review of the literature. 2005, Hum Exp Toxicol, 24:27-33.

#### Thursday, February 11, 2010

**Question:**

What is the most common form of human botulism in the United States and what is the mechanism for the development of this form of botulism?

**Answer:**

The most common form of human botulism in the United States is infant botulism, sometimes known as intestinal toxemia. Spores of *Clostridium botulinum* (or uncommonly, neurotoxicogenic *C. butyricum* or *C. baratii*) are swallowed and then germinate and colonize the lumen of the large intestine, where they produce botulinum neurotoxin. The toxin is absorbed and travels via the bloodstream to the neuromuscular junction and binds at that site irreversibly. Laboratory-confirmed cases range from mild, outpatient illness to sudden, fatal respiratory arrest. However, the majority of all cases in the United States (approximately 100 annually) are identified because their severity results in hospital admission. (Armon SS, et al. Human botulism immune globulin for the treatment of infant botulism, 2006, NEJM, 354(5):462-471)

#### Wednesday, February 10, 2010

**Question:**

As the Northeast U.S. is being pelted by a record number of snow storms this winter, how does the application of road salt for de-icing snowy streets influence the possibility of carbon monoxide (CO) poisoning during the winter months?

**Answer:**

The answer is found in a phenomenon known as "CO burnout" involving fires in underground utility lines. Underground fires typically begin when the rubber coating of utility cables crack and split because of normal wear and tear, freezing and thawing, and excavation. As the cable insulation is breached, water (i.e., rain or runoff) and road salt from de-icing cause electrical shorts and underground fires. The burning cable and insulation creates noxious emissions containing CO. The CO gas released travels along conduits under streets and ultimately migrates into residential, commercial, and industrial settings. Smoke and CO also can be emitted from utility portals (i.e., "manholes") and drawn into nearby buildings through ventilation systems. As more lines are buried, CO burnouts might increase in frequency. Anecdotal information recorded in the HSEES (Hazardous Substances Emergency Events Surveillance system) system suggests that these events often occur when road salt is applied for de-icing after large snow or ice storms. Before several CO burnout events in December, 2003, approximately 105,000 tons of salt were spread on New York City streets after a snowstorm. The utility company reported that rock salt penetrated into underground electrical cables, leading to fires and CO releases several days later. (MMWR, October 8, 2004/ 53(39): 920-922)



**Tuesday, February 9, 2010****Question:**

What is compound 1080?

**Answer:**

Compound 1080 is sodium monofluoroacetate (SMFA), a material used as a rodenticide and coyotocide until it was banned in the US in 1972. Poisoning by this material may be characterized by the presence of a high anion gap metabolic acidosis. Compound 1080 was often formulated for use in "livestock protection" collars. The collars, worn by sheep, goats and other livestock, were intended to control coyotes that prey on such animals. (Robinson RF, et al. Intoxication with sodium monofluoroacetate (compound 1080). 2002, Vet and Human Tox. 44(2): 93-95)

**Monday, February 8, 2010****Question:**

Which zoonotic infection (a CDC category B agent), feared as a potential weapon that may be used by terrorists, is caused by an obligate, intracellular, gram negative organism that may infect a variety of hosts including humans, reptiles, ruminants, reptiles and birds and can be spread from animal products of conception? What is the treatment recommended for this infection in humans?

**Answer:**

Q fever is the infection and is caused by the bacteria *Coxiella burnetii*. Humans may be exposed to the disease as other animals shed the organism in feces, urine, milk, and products of conception. These materials, especially post partum products, contain large numbers of *Coxiella* organisms that can become aerosolized after drying and may remain virulent for many months. Recommended therapy includes doxycycline or quinolone antibiotics. (Hartzell JD, et al. Q fever: Epidemiology, diagnosis, and treatment. 2008. Mayo Clinic Proceedings 83(5):574-579)

**Friday, February 5, 2010****Question:**

What does the acronym "EMLA" stand for and what are the constituents of this topical anesthetic agent?

**Answer:**

"EMLA" stands for "eutectic mixture of local anesthetics". [A "eutectic mixture" is mixture of chemicals that has a single chemical composition and solidifies at a lower temperature than any other composition.] EMLA consists of prilocaine (2.5%) and lidocaine (2.5%) and was the first commercially available topical anesthetic agent shown to provide adequate analgesic efficacy. (Eidelman A, et al. Topical anesthetics for dermal instrumentation: A systematic review of randomized, controlled trials. 2005, Ann Emerg Med, 46:343-351.)

**Thursday, February 4, 2010****Question:**

What is *Salvia divinorum*, what is the toxin of concern contained therein, and what is the biological effect of this toxin? What are some popular street names for *Salvia divinorum*?

**Answer:**

*S. divinorum* is a plant from the Sage family that has been used in traditional spiritual and ethnopharmacological practices by the Mazatec Indians of Oaxaca, Mexico to produce mystical or hallucinogenic experiences. Currently, *S. divinorum* is unregulated in most countries and widely available via the internet. It is a controlled substance in Denmark, Australia, and Italy. To date, Federal U.S. laws for controlled substances do not ban the use of *S. divinorum* or its active components however a number of states have enacted legal control for this substance. The active constituent in *S. divinorum* is the diterpene salvinorin A. A smoked dose of *S. divinorum* in humans can produce profound hallucinations lasting approximately 30-60 minutes. Street names for *Salvia* include: Maria Pastora, Sage of the Seers, Diviners Sage, *Salvia*, Sally-D, and Magic Mint. (Prisinzano TE. Psychopharmacology of the hallucinogenic sage *Salvia divinorum*. 2005, Life Sciences, 78:527-531) also see: [http://www.justice.gov/dea/concern/salvia\\_divinorum\\_and\\_salvinorin\\_A\\_November\\_2008\\_first\\_fact.pdf](http://www.justice.gov/dea/concern/salvia_divinorum_and_salvinorin_A_November_2008_first_fact.pdf)

**Wednesday, February 3, 2010****Question:**

N,N-Dimethylformamide (DMF) is an industrial solvent commonly used in the manufacture of films, fibers, coatings and polyurethane lacquers. Worldwide production of DMF is estimated to be in the range of 250,000 tons per year. What are the routes of concern for occupational exposure to DMF in humans, what potential toxicity is of most concern in workers and is DMF considered to be a human carcinogen?

**Answer:**

Human occupational exposure to DMF may occur via inhalation and/or dermal absorption. The main toxicities of concern involve the potential for GI irritation and/or hepatotoxicity. Although no increase has been found in the incidence of cancer in humans in large epidemiological studies, some studies have reported on a possible association (unconfirmed) with testicular germ-cell tumors among workers who may have been exposed to DMF. DMF has been classified as group 2B (possibly carcinogenic to humans) by the International Agency for Research on Cancer (IARC). US EPA has not classified DMF with regard to possible carcinogenicity. (Kafferlein HU, et al. Biological monitoring of workers exposed to N,N-dimethylformamide in the synthetic fiber industry. 2000. Int Arch Occup Environ Health, 73:113-120)

**Tuesday, February 2, 2010****Question:**

Exposure to high levels of fluoride can cause symptoms ranging from discoloration of teeth in children to severe osteoarthritis in adults. One potentially dangerous, but under-recognized, source of fluoride is tea. Tea trees accumulate and store fluoride, absorbing it selectively from the air and soil with up to 98% of the fluoride stored in the leaves of the tree. Which tea is of most concern with regard to the potential for exposure to high fluoride levels and what commercial form of this tea is of most concern?

**Answer:**

One study of a variety of teas revealed wide differences in fluoride levels. The fluoride content was found to be 0.951.41 mg/L in black tea sticks, 0.702.44 mg/L in black tea granules and 1.156.01 mg/L in black tea bags. Of the products tested, the fluoride content was greatest in black tea bags, presumably because black tea bags are made of low cost, and older tea leaves. According to the World Health Organization's (WHO) recommendation, the fluoride exposure threshold for children is 2 mg of daily intake and for adult, 4 mg. Thus, even moderate daily intakes of this tea (which occur routinely in some cultures domestically as well as internationally) may be unsafe and according to the WHO, could result in an increased risk of osteofluorosis and fractures. (Cao J, et al. Fluoride levels in various black tea commodities: Measurement and safety evaluation. 2006. Food and Chemical Toxicology, 44: 11131-1137)

**Monday, February 1, 2010****Question:**

A recent review discussed the fact that hospitalized patients often receive in-appropriately prescribed vancomycin. Some studies reveal inappropriate use of vancomycin in up to 50% (or more) of patients, even when culture results were available. What are the most common inappropriate uses of vancomycin therapy in hospitalized patients?

**Answer:**

The most common inappropriate uses in hospitalized patients involved vancomycin therapy for surgical prophylaxis or continued administration of vancomycin after cultures were negative for beta-lactamresistant Gram-positive bacteria. (Levine DP. Vancomycin: understanding its past and preserving its future. 2008. Southern Med J, 101(3):284-291).

**Friday, January 29, 2010****Question:**

Removal of baclofen from individuals with long-term dependence on intrathecal delivery of this drug may be associated with a potentially fatal syndrome that generally develops over 24 to 72 hours. What clinical findings characterize this baclofen withdrawal syndrome and what are the most common causes for this syndrome?

**Answer:**

The baclofen withdrawal syndrome may include rebound spasticity, hemodynamic lability, severe hyperthermia, and altered mental status. Common descriptions of patients who have developed this syndrome involve routine pump malfunction secondary to catheter kinking or programming errors leading to inadequate and inaccurate delivery and dosing of intrathecal baclofen. (Douglas AF, et al. Prolonged intrathecal baclofen withdrawal syndrome. 2005, J Neurosurg 102:1133-1136)

**Thursday, January 28, 2010****Question:**

In 2006, the CDC's Morbidity Mortality Weekly Report published information regarding a number of deaths that were related to chelation treatment of several children. What was the cause of the deaths described and what chelating agent was determined to be responsible?

**Answer:**

The cases reported in the MMWR issue cited below involved chelation therapy-related hypocalcemia causing cardiac arrest. In at least two of the reported cases, the drug Na2EDTA was administered and was designated as the cause for lethal hypocalcemia in these cases. In at least one of the reported cases the intention may have been to administer CaEDTA but Na2EDTA was given in error. The safety and effectiveness of Na2EDTA has not been established for pediatric patients and it should not be used in children because of its propensity to cause severe, life-threatening, hypocalcemia. (MMWR, "Deaths associated with hypocalcemia from chelation therapy---Texas, Pennsylvania, and Oregon, 2003-2005", March 3,2006/ 55(08):204-207).

**Wednesday, January 27, 2010**

**Question:**

It is well publicized that snorting cocaine can destroy the nasal mucosa and cartilaginous septum, but the evidence indicates that septal erosion is not as common as public perception would have it. What is the rate of septal perforation as a result of snorting cocaine?

**Answer:**

Septal perforation as a sequelae of snorting cocaine is generally quoted at a rate of just less than 5 % amongst regular cocaine (powder) abusers. However, it is likely that all figures relating to nasal destruction from cocaine abuse are, in reality, under reported and the actual rate may be higher than 5%. (Harper SJ, Jones NS. "Cocaine: what role does it have in current ENT practice? A review of the current literature". J Laryngology & Otology, 2006; 120: 808-811.

**Tuesday, January 26, 2010**

**Question:**

Carbon monoxide (CO) can be formed when certain anesthetic agents are used with anesthetic breathing systems containing carbon dioxide (CO2) absorbents. Which anesthetics have been associated with this potentially life-threatening phenomenon and what is the proposed mechanism for this untoward event?

**Answer:**

The volatile anesthetic agents that may break down to form CO include desflurane, sevoflurane, enflurane and isoflurane. This phenomenon occurs when the carbon dioxide absorbent in the anesthesia machine system is not properly maintained and is allowed to dry out. The production of CO is based on the chemical degradation of the above agents and that degradation has been noted to be inversely related to the water content of the absorbent in the system. The typical case of CO poisoning in this setting has been deemed "Monday morning disease" as the first patient undergoing surgery on Monday morning is the classic patient afflicted when, after the weekend, an anesthesia machine is used through which high gas flows had been maintained during the previous week or weekend resulting in drying of the absorbent. For these reasons, and others, some of these inhalational agents are falling out of favor but most are still widely used in both human and veterinary anesthesia (Coppens MJ, et al. The mechanisms of carbon monoxide production by inhalational agents. 2006; Anesthesia, 61:462-468)

**Monday, January 25, 2010**

**Question:**

Included among America's first workers exposed to radioactivity were approximately 2000 teenage girls and young women hired during World War I to apply luminous numbers on watch and instrument dials with paint that contained radium. How were these women exposed to radium as a result of their occupational activities?

**Answer:**

These unfortunate individuals were exposed to radium through licking their paint brushes to attain a fine point, through inhaling fine particles of radium-laden dust and radon, and through exposure to high levels of gamma radiation. The dialpainters were among America's first industrial victims of radiation poisoning. Some of the manifestations of radium poisoning experienced by these women included osteonecrosis of the mandible as well as various blood dyscrasias and leukemias (Clark C. Physicians, reformers and occupational disease: The discovery of radium poisoning. 1987, Women & Health, 12(2):147-167.)

**Friday, January 22, 2010**

**Question:**

At least 11 states, including Alaska, California, Colorado, Hawaii, Maine, Montana, Nevada, New Mexico, Oregon, Rhode Island, Vermont and Washington currently allow marijuana use for certain limited medical purposes. What are the various forms of "medical marijuana" currently available?

**Answer:**

The forms of marijuana currently available for legal medical use in the US or Canada include the following. 1- botanical marijuana; the marijuana plant itself. 2- synthetic oral cannabinoids; dronabinol (Marinol) and nabilone (Cesamet), both approved by the US FDA for more than 20 years to treat nausea associated with chemotherapy and unresponsive to standard anti-emetic agents. 3- oral/mucosal spray; nabiximols- (Sativex). (The Medical Letter, 2010, 52(1330):5) see also (Seamon MJ, et al. Medical marijuana and the developing role of the pharmacist. American J Health System Pharmacy,2007, 64(10):1037-1044).

**Thursday, January 21, 2010**

**Question:**

At least 11 states, including Alaska, California, Colorado, Hawaii, Maine, Montana, Nevada, New Mexico, Oregon, Rhode Island, Vermont and Washington currently allow marijuana use for certain limited medical purposes. What are the various forms of "medical marijuana" currently available?

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The forms of marijuana currently available for legal medical use in the US or Canada include the following. 1- botanical marijuana; the marijuana plant itself. 2- synthetic oral cannabinoids; dronabinol (Marinol) and nabilone (Cesamet), both approved by the US FDA for more than 20 years to treat nausea associated with chemotherapy and unresponsive to standard anti-emetic agents. 3- oral/mucosal spray; nabiximols- (Sativex). (The Medical Letter, 2010, 52(1330):5) see also (Seamon MJ, et al. Medical marijuana and the developing role of the pharmacist. American J Health System Pharmacy,2007, 64(10):1037-1044).

**Thursday, January 21, 2010**

**Question:**

It is believed that as many as 13 million Americans suffer from ocular cataracts. Cataract formation is a multifactorial process that some believe to be initiated by oxidative stress and injury from oxygen radicals. What group of drugs, widely prescribed for the treatment of dyslipidemias, have a preventive effect against cataract formation in humans?

**Answer:**

Persistent use of the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statin drugs) has recently been shown to be significantly protective for the incidence of cataract formation in men and women under 75 years of age but not necessarily in those older than 75 years of age. (Chodick G, et al. Persistence with statins and incident cataract: A population based historical cohort study. 2009, Annals of Epidemiology, 20(2):136-142)

**Wednesday, January 20, 2010**

**Question:**

In 1990 it was discovered that a specific bird contained, in its feathers and muscle tissue, a chemical toxin that caused numbness, burning and sneezing on contact with human buccal and nasal tissues during collection and preparation of specimens of these animals. What bird does this describe and what is the toxin at issue?

**Answer:**

The bird is the hooded pitohui, Pitohui dichrous (as well as other Pitohui species....although P. dichrous contains the highest concentration of toxin). The toxin was identified as homobatrachotoxin, a member of a family of steroidal alkaloids collectively known as batrachotoxins. Batrachotoxins depolarize nerve and muscle cells by activating sodium channels and thus irritate sensory neurons in buccal tissue. (Dumbacher JP, et al. Homobatrachotoxin in the genus Pitohui: Chemical defense in birds? 1992, Science, 258:799-800)

**Tuesday, January 19, 2010**

**Question:**

What is the Irukandji syndrome?

**Answer:**

The Irukandji syndrome, named after a local Aboriginal tribe, was first described in Australia by Flecker in the early 1950's. Irukandji syndrome is a clinical syndrome comprised of hypercatecholaminergic symptoms due to jellyfish envenomation by the small box jellyfish Carukia barnesi. This syndrome is highly variable but classically includes severe generalized pain and distress that may occur in conjunction with hypertension, cardiomyopathy and cardiogenic pulmonary edema. Fatal outcomes due to the Irukandji syndrome have been reported. (Macrokanis CJ, et al. Irukandji syndrome on northern Western Australia: an emerging health problem. Med J Australia, 2004; 181(11/12):699-702)

**Monday, January 18, 2010**

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**Question:**

A recent discussion in The Medical Letter concluded that intravenous ibuprofen reduces pain and may have a limited but potentially clinically important opioid sparing effect in patients who are unable to take oral medications following surgery. What are the potential adverse effects associated with the use of IV ibuprofen?

**Answer:**

A double-blind study of more than 400 post operative patients compared adding IV ibuprofen versus placebo to "prn" morphine for post-op pain. In this study the only adverse effect occurring more frequently with IV ibuprofen than with placebo was dizziness (9% versus 1%). It is important to note that ibuprofen inhibits platelet function and NSAIDs are contraindicated in patients undergoing coronary bypass surgery. Some orthopedic surgeons believe that ibuprofen used post-operatively may interfere with bone healing. Long-term use of oral ibuprofen has been associated with GI and renal toxicity. (The Medical Letter, January 11, 2010, 52(1329):3-4) see also (Southworth S., et al. A multi-center, randomized, double blinded, placebo controlled trial of intravenous ibuprofen 400 and 800 mg every 6 hours in the management of postoperative pain. (Clinical Therapeutics, 2009; 31(9):1922-1935.)

**Friday, January 15, 2010****Question:**

During the past 7 decades, at least 12 documented occurrences of diethylene glycol contamination of medications have resulted in at least 450 deaths. These poisoning epidemics have occurred primarily in developing countries and have been associated with inadequate adherence to safe manufacturing practices, lack of enforcement of safe practices, or what appear to be intentionally deceptive drug manufacturing practices. What is the clinical hallmark of DEG poisoning?

**Answer:**

The hallmark of DEG poisoning is acute renal failure. (MMWR, Fatal poisoning among young children from diethylene glycol contaminated acetaminophen-Nigeria, 2008-2009. December 11, 2009. 58(48): 1345-1347.)

**Thursday, January 14, 2010****Question:**

What is PFOA?

**Answer:**

Perfluorooctanoate (PFOA) is a perfluorinated carboxylate that finds commercial use as a surface-active agent in the production of a variety of fluoropolymers. PFOA is a peroxisome proliferator and has been associated with the development of hepatocellular tumors, Leydig cell tumors and pancreatic acinar cell tumors in some lab animals under experimental conditions. It has not, however, been shown to cause these tumors in humans. (Kennedy GL, et al. The toxicology of perfluorooctanoate. 2004. Crit Rev in Tox 34(4):351-384)

**Wednesday, January 13, 2010****Question:**

Ocular pain, lacrimation, blepharospasm, photophobia, and blindness are the major ophthalmic effects associated with significant acute ocular exposure to sulfur mustard gas or vapor. What are the reported potential long-term sequelae associated with exposure to sulfur mustard gas or vapor?

**Answer:**

According to the paper cited below, decades following initial exposure, many World War I veterans experienced delayed keratitis, photophobia, and pain after having healthy eyesight post-exposure. More recently, as many as 15% of exposed Iranian soldiers have reportedly been diagnosed with delayed keratitis. This delayed injury has revealed itself between 15 and 20 years after exposure but has had latency periods reported as early as 1 year and as late as 40 years. Other long-term ocular sequelae include itching, ocular burning, photophobia, tearing, presbyopia with reading difficulties, eye pain, and foreign body sensations. (Geraci MJ. Mustard gas: Imminent danger or eminent threat? 2008, Ann Pharmacotherapy 42(2):237-24

**Tuesday, January 12, 2010****Question:**

What are the clinical consequences of metal ions that may be released from orthopedic implants in humans?

**Answer:**

According to the article cited below, the consequences of metal ion release from orthopedic implants are unclear; but several concerns have been raised, as follows: (1) It has been suggested that local effects of metal ions include induction of polyethylene- independent, lymphocyte-mediated osteolysis; and it has been described that cobalt ions inhibit osteoblast proliferation and collagen synthesis. (2) Toxicologic considerations imply that the mutagenicity of heavy metal ions can increase the risk of cancer, although no significant elevation of the risk ratio for malignant diseases has been described to date. (3) Immunologic changes such as a decrease in the amount of a subset of lymphocytes have been observed in patients with elevated metal ion levels subsequent to metal-on- metal alloarthroplasty, and some metal ions such as nickel and chromium are well known to induce allergic reactions. (Dahlstrand H, et al. Elevated Serum Concentrations of Cobalt, Chromium, Nickel, and Manganese After Metal-On-Metal Alloarthroplasty of the Hip: A Prospective Randomized Study. 2009. The Journal of Arthroplasty, 24(6): 837-845.)

**Monday, January 11, 2010****Question:**

What are the potential long-term complications commonly discussed with regard to survivors of exotic snake bites?

**Answer:**

At the site of the bite, loss of tissue may result from sloughing or surgical débridement of necrotic areas or as a result of surgical amputation. In addition, chronic ulceration, infection, osteomyelitis or arthritis may persist causing severe physical disability. Malignant transformation has been reported to occur in skin ulcers at the site of healed bites after a number of years. Chronic renal failure occurs after bilateral cortical necrosis (specifically with Russells viper bites) and chronic panhypopituitarism as well as diabetes insipidus have been reported following Russells viper bites. Chronic neurological deficits may be seen in the few patients who survive intracranial hemorrhages related to post bite coagulopathy. (World Health Organization, 2005. Guidelines for the Clinical Management of Snake Bite in the South-East Asia Region: [http://www.searo.who.int/LinkFiles/SDE\\_mgmt\\_snake-bite.pdf](http://www.searo.who.int/LinkFiles/SDE_mgmt_snake-bite.pdf)) and (Warrell DA. Snake bite. 2009. The Lancet, 375 (9708):77-88)

**Friday, January 8, 2010****Question:**

What two general categories of respiratory illness may result from occupational exposure to beryllium and what are the general proposed causative mechanisms?

**Answer:**

Exposure to beryllium may result in two specific and distinct respiratory conditions; acute beryllium disease (ABD) and chronic beryllium disease (CBD). ABD has generally been regarded to be related to an irritative effect of inhaled beryllium, however recent theories point to a probable immune mediated component as well for ABD. CBD is generally believed to be an immune mediated granulomatous process. (Cummings KJ, et al. A reconsideration of acute beryllium disease. 2009. Environ Health Perspectives 117(8):1250-1256)

**Thursday, January 7, 2010****Question:**

What is organotin and what are the usual industrial uses for these compounds?

**Answer:**

Organotins are a group of chemical compounds, also known as stannanes, having the element tin as part of the chemical base with various hydrocarbons added depending on the specific compound. Organotins have been widely used in a variety of industrial and agricultural applications including as slime inhibitors, mildew proofing agents, polyvinyl chloride stabilizers, and biocides. Organotin, specifically, tributyltin, has been widely used as a biocide agent in antifouling paints used to paint the hulls of ships. Due to the potential threat these compounds might pose to marine environments, the use of organotins in antifouling paints has been banned in many countries in Europe and in North America. (Cao D, et al. Organotin pollution in China: An overview of the current state and potential health risk. 2009. 90:516-524)

**Wednesday, January 6, 2010****Question:**

What is "blackfoot disease", why has it been given this rather unique name, and what environmental exposure has been suggested as the cause based on a variety of epidemiological studies?

**Answer:**

Blackfoot disease (BFD) is a unique peripheral vascular disease reported to be endemic in a circumscribed area located at the southwestern coast of Taiwan. Blackfoot disease was so named due to the noted characteristic progression from numbness/coldness of the lower extremities to intermittent claudication and finally to gangrene and spontaneous amputation. Epidemiologic studies have linked the etiology of BFD to the ingestion of local artesian well water. Arsenic, ergot alkaloid, organic chlorides, and humic acid have been identified in the water. In addition, trace elements, such as molybdenum, mercury, copper, and cadmium, were reported to be detectable in the serum and/or urine of BFD patients and in ground water they used. However, extensive epidemiologic studies favor arsenic as the most probable cause for BFD. The specific role of arsenic is unclear but probably involves arsenic's atherogenicity causing peripheral vascular insufficiency and/or its association with hypertension and diabetes mellitus causing peripheral microangiopathy. (Tseng CH. An overview on peripheral vascular disease in blackfoot disease- hyperendemic villages in Taiwan. 2002. Angiology 53(5):529-537.)

**Tuesday, January 5, 2010**

**Question:**

Red yeast rice (RYR) is a substance that is formed when rice is fermented with the yeast *Monascus purpureus*. It is used by many seeking "alternative medicines" for lowering serum cholesterol levels. Part 1-How does RYR lower cholesterol? Part 2-What are the potential adverse effects associated with RYR?

**Answer:**

Part 1- Approximately 75% of the antihyperlipidemic activity of red yeast rice is most likely attributable to the lactone and hydroxy-acid forms of monacolin K, a metabolite of *Monascus purpureus* that inhibits 3-hydroxy-3-methyl- glutaryl coenzyme A (HMG-CoA) reductase. In 1979, monacolin K and lovastatin (then known as mevinolin) were recognized to be identical compounds. Five milligrams of monacolin K has been shown to be the approximate equivalent of 20-40 mg of lovastatin. (Grieco A, et al. Acute hepatitis caused by a natural lipid lowering product: When "alternative" medicine is no "alternative" at all. 2009, Journal of Hepatology, 50:1273-1277. Part 2- RYR use can trigger myopathy in the same way that any statin drug can. Rhabdomyolysis has been reported as well in a patient taking RYR in conjunction with cyclosporine. RYR has also been reported to cause acute hepatitis. Some products advertised as "Red Yeast Rice" may contain citrinin, a mycotoxin that can cause renal failure in animals. In addition, statins (and thus RYR) are teratogenic in animals and should not be taken during pregnancy. (The Medical Letter. September,2009. 51(1320):71-72)

**Monday, January 4, 2010**

**Question:**

What is a "DRE"? (no..... it's NOT a "digital rectal exam")

**Answer:**

A DRE is a police officer trained and certified as a Drug Recognition Expert. The Drug Recognition Expert (DRE) Program and procedures were initially developed in the 1970s by traffic enforcement officers of the Los Angeles Police Department. This procedure trains selected officers to utilize a standardized twelve step evaluation procedure, that enables the officer to determine whether an individual is under the influence of drugs, and then to determine the type of drug causing the observable impairment. Importantly, the DRE procedure enables the DRE to rule in (or out) many medical conditions, such as illness or injury, that may be contributing to the impairment. Although the primary focus of the DRE procedure is driving under the influence (DUI) enforcement, the procedures have been applied to Health and Safety Code violations, probation, parole, drugs in the workplace issues, and other areas where accurately identifying the drug-impaired individual is relevant. The accuracy of the procedure used by DREs has been validated in two controlled studies. In 1984, a research study at Johns Hopkins University showed that Los Angeles DREs were able to accurately distinguish between the drug-impaired and non-drug-impaired individual. A subsequent Field Validation Study (173 case study) sponsored by the National Highway Traffic Safety Administration in 1985 evaluated the accuracy of the DRE procedures in actual arrest situations. Again, the DREs were very successful in identifying both the drug-impaired individual and the class(es) of drug(s) causing the impairment. DRE procedures have been subject to numerous defense motions challenging the admissibility of DRE testimony. Thus far, courts in California, New York, Arizona, Minnesota, Colorado, and Florida have upheld the admissibility of DRE evidence. As an example of DRE's acceptance in court, the Los Angeles City Attorneys Office has estimated that 95% of those charged with driving under the influence of drugs are convicted in LA courts. Today, approximately 4,000 nationwide are certified as DREs by the International Association of Chiefs of Police (IACP). All DREs can trace their expertise back to the 16 Los Angeles DREs that developed the initial formal curriculum in 1986. It has been through the continued involvement of the LAPD that DRE has achieved its international stature. (<http://www.ci.la.ca.us/LAPD/traffic/dre/overview.htm>)

**Thursday, December 31, 2009**

**Question:**

There are currently three insulin analogs classified as rapidly acting agents available in the United States: insulin lispro (Humalog), insulin aspart (Novolog), and insulin glulisine (Apidra). How do these insulin analogs compare with regular insulin with regard to postprandial hyperglycemia, effects on HgB A1C, and nocturnal hypoglycemia?

**Answer:**

According to a discussion published in The Medical Letter, all three insulin analogs are more effective than regular insulin in decreasing postprandial hyperglycemia however they decrease HgB A1C only slightly more than regular insulin. With regard to nocturnal hypoglycemia, when compared with regular insulin, all three decrease nocturnal hypoglycemia. (The Medical Letter, 2009, 51 (1327/1328):98.)

**Wednesday, December 30, 2009**

**Question:**

Is it safe to use drugs that have past the expiration date on the label of the bottle in which they were dispensed?

**Answer:**

According to a recent discussion of this question in the publication "The Medical Letter", "when no suitable alternative is available, outdated drugs may be effective, and there is no indication that they are not safe". This discussion concluded that while there are no reports of toxicity from degradation products of currently available drugs, the amount of drug potency retained after "expiration" varies with the drug, the lot, and the storage conditions, especially humidity. They go on to note that "many drugs stored under reasonable conditions in their original unopened containers retain 90% of their potency for at least 5 years after the expiration date on the label, and sometimes much longer." Epinephrine in EpiPen is a notable exception as this product loses substantial potency after its expiration date. One study reported a decrease in epinephrine content in the EpiPen inversely proportional to the number of months past the expiration date on the label. (The Medical Letter, 2009, 51 (1327/1328):100-101)

**Tuesday, December 29, 2009**

**Question:**

What is henna and what is the current popular use for this substance?

**Answer:**

Henna (*Lawsonia inermis*) is a deciduous shrub with acuminate leaves. Henna is a member of the family Lythraceae. Members of this family are known as a source of natural dyes. The flowers of henna plants are yellowish white to brick red, and the fruit is a dry berry. The seeds are blue-black, angular, and small. The active ingredient of henna is lawsone (2-hydroxy-1,4-naphthoquinone). Decorating one's hands and feet with henna is a traditional custom for events such as wedding parties and public celebrations in the Middle East and other areas around the world. The dried leaves are ground into a fine powder and mixed with water or oil to create a paste. This paste is applied directly to the skin with a cone-shaped, soft container and left to dry for 20 to 30 minutes. These temporary henna tattoos are called mehndi and remain visible for 2 to 4 weeks. Mehndi are used as a reminder of happiness, as a form of blessing for the wearer, and depending on its intent, are used for its aphrodisiac quality. Recently, temporary henna tattoos have become increasingly popular and this has been accompanied by an increased rate of allergic reactions despite the fact that henna generally is regarded as having a rather low allergic potential. (Kazandjieva J, et al. Temporary henna tattoos. 2007, Clinics in Dermatology 25(4):383-387)

**Monday, December 28, 2009**

**Question:**

Contamination of which illicit drugs with the veterinary anti-helminthic agent, levamisole, has recently been linked to the development of what hematologic disorder?

**Answer:**

The hematologic disorder is agranulocytosis and it has been reported in some individuals using cocaine but it has also been reported in some heroin users. To date only trace amounts of levamisole have been detected in contaminated heroin samples while cocaine samples contaminated with levamisole reportedly contained an average concentration of approximately 10% levamisole. (MMWR, Dec 18,2009, 58(49):1381-1384)

**Thursday, December 24, 2009**

**Question:**

Is there a specific medical test for DES exposure for patients who may not know for sure if their parents were exposed to DES?

**Answer:**

No known medical test (such as blood, urine or skin analysis) has been developed that can detect DES exposure. However, the DES Self-Assessment Guide is designed to help assess if an individual might have been exposed to DES. For information regarding the DES Self-Assessment Guide go to: <http://www.cdc.gov/des/consumers/guide/index.html>

**Wednesday, December 23, 2009**

**Question:**

Do the children of DES Daughters and Sons have any health risks?

**Answer:**

Third-generation children (the offspring of DES Daughters and Sons) are just beginning to reach the age when relevant health problems (such as reproductive tract problems), can be studied. A study of the health risks for the granddaughters of women prescribed DES while pregnant, or third-generation daughters, was published in 2002. The researchers compared findings of pelvic examinations of 28 DES Granddaughters with findings noted in their mothers (DES Daughters). Even though abnormalities were present in more than 60% of DES Daughters, no abnormalities were found in the DES Granddaughters (Kaufman RH, Adam E. Findings in female offspring of women exposed in utero to diethylstilbestrol. *Obstet Gynecol* 2002;99:197-200.) DES Grandsons are being studied at the Netherlands Cancer Institute. Early research reported that hypospadias, misplaced opening of the penis, occurred 20 times more frequently among sons of DES Daughters (Klip H, et al. Hypospadias in sons of women exposed to diethylstilbestrol in utero: a cohort study. *Lancet* 2002;359:1102-7) ([http://www.cdc.gov/des/consumers/about/concerns\\_offspring.html](http://www.cdc.gov/des/consumers/about/concerns_offspring.html))

**Tuesday, December 22, 2009**

**Question:**

"DES Daughters" are defined as women born between 1938 and 1971 who were exposed to DES (Diethylstilbestrol) before birth (in the womb). Research has confirmed that DES Daughters are at an increased risk for: Clear cell adenocarcinoma (CCA), Reproductive tract structural differences (for example, T-shaped uterus), Pregnancy complications, such as ectopic (tubal) pregnancy and pre-term delivery and Infertility. What are the increased risks for "DES Sons"?

**Answer:**

"DES Sons" are defined as men born between 1938 and 1971 who were exposed to DES before birth (in the womb). Research has confirmed that DES Sons are at an increased risk for: Non-cancerous epididymal cysts but no other abnormalities or increased incidence of cancers (<http://www.cdc.gov/des/consumers/sons/index.html>)

**Monday, December 21, 2009**

**Question:**

What is the chemical abbreviated as "DES" and what was it used for?

**Answer:**

Diethylstilbestrol (DES) is an estrogen that was first manufactured in a laboratory in 1938, so it is called a "synthetic estrogen." During 1938-1971, U.S. physicians prescribed DES to pregnant women to prevent miscarriages and avoid other pregnancy problems. As a result, an estimated 5-10 million pregnant women and the children born of these pregnancies were exposed to DES. Physicians prescribed DES to pregnant women on the theory that miscarriages and premature births occurred because some pregnant women did not produce enough estrogen naturally. At the time, physicians thought DES was safe and would prevent miscarriages and pre-term (early) births. (<http://www.cdc.gov/des/consumers/about/index.html>)

**Friday, December 18, 2009**

**Question:**

The substance known as Spanish fly has been used historically as an aphrodisiac based on its effects as a urinary-tract irritant capable of inducing genital swelling and priapism. What is the active constituent of Spanish fly and what is its potential toxicity following ingestion?

**Answer:**

Spanish fly is a powder derived from the blister beetle *Cantharis vesicatoria*. The active ingredient in "Spanish fly" is cantharidin. Skin contact with cantharidin from male blister beetles can cause painful blisters while ingestion of as little as 10 mg of pure cantharidin has reportedly caused death in an adult human. It is thought that cantharidin inhibits protein phosphatases types 1 and 2A, increasing capillary permeability to albumin and leading to diffuse endothelial injury with consequent edema, inflammation, vesication, and, after ingestion, gastrointestinal hemorrhage and hematuria. (Tagwireyi D, et al. Cantharidin poisoning due to Blister beetle ingestion. *Toxicol* 2000; 38(12):1865-1869.) - James M. Madsen, MD, MPH, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; [zmaddoc@gmail.com](mailto:zmaddoc@gmail.com)

**Thursday, December 17, 2009**

**Question:**

Chronic occupational exposure to carbon disulfide has been reported to cause accelerated atherosclerotic coronary artery disease, retinal microaneurysms and peripheral neuropathy with ascending symmetrical paresthesias and weakness. What is the occupational setting where carbon disulfide exposure has usually been reported?

**Answer:**

Carbon disulfide (CS<sub>2</sub>) is used in the manufacture of viscose rayon and most exposures discussed in the literature have occurred in workers in this industry. (Chang S-J, et al. Electrocardiographic abnormality for workers exposed to carbon disulfide at a viscose rayon plant. *J Occ Env Med*, 2006, 48(4):394-399)- James Madsen, MD, MPH, Fellow in Medical Toxicology, Drexel Univ. Coll of Med, Philadelphia, PA; [zmaddoc@gmail.com](mailto:zmaddoc@gmail.com))

**Wednesday, December 16, 2009**

**Question:**

Amiodarone is a benzofuran antiarrhythmic drug with a substantial adverse effect profile, that may involve the liver, thyroid, cornea, skin, and neuromuscular system, and which often limits its use. Pulmonary toxicity related to amiodarone was first described in the early 1980s and is sometimes called amiodarone pneumonitis or amiodarone lung. When does this disorder typically develop, what is the population prevalence for this complication of therapy, and how is this disorder diagnosed?

**Answer:**

In some cases amiodarone pneumonitis has developed within days of starting treatment while in other cases manifestations have been delayed for up to ten years. However, in most cases, amiodarone pulmonary toxicity develops during the first 18 months of therapy. The cumulative prevalence for amiodarone related pulmonary toxicity ranges between 1% and 15% of the treated population. Although the disease typically is asymmetrical on imaging, the patterns of amiodarone pneumonitis are varied and mis-diagnosis is common. In the absence of biopsy proven disease, the diagnosis is usually one of exclusion. (Camus P, et al. Amiodarone pulmonary toxicity, 2004, *Clin Chest Med* 25:65-75)

**Tuesday, December 15, 2009**

**Question:**

What is epidemic dropsy, where does it occur, and what is responsible for this condition?

**Answer:**

Epidemic dropsy is a multisystem condition caused by the consumption, usually in adulterated mustard oil, of argemone seed, from the Mexican prickly poppy (*Argemone mexicana*). Argemone-oil poisoning is characterized by gastrointestinal signs and symptoms (nausea, vomiting, and diarrhea), erythema, headache, breathlessness, bilateral pitting edema, and visual-field defects and is most common in India, Mauritius, Fiji, and South Africa. Sanguinarine and dihydrosanguinarine, two benzophenanthridine alkaloids found in *A. mexicana*, decrease active transport of glucose and inactive glycogenolysis, leading to the accumulation of pyruvate and uncoupling of oxidative phosphorylation. (Das M, Khanna S. Clinicoepidemiological, Toxicological, and Safety Evaluation Studies on Argemone Oil. *Critical Reviews in Toxicology* 1997; 27(3):273-297; and Singh K, Singh MJ, Das JC. Visual Field Defects in Epidemic Dropsy. *Clinical Toxicology* 2006; 44(2):159-163.) - James M. Madsen, MD, MPH, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; [zmaddoc@gmail.com](mailto:zmaddoc@gmail.com)

**Monday, December 14, 2009**

**Question:**

What is the Globally Harmonized System (GHS) and how does it relate to toxicology?

**Answer:**

The Globally Harmonized System of Classification and Labelling of Chemicals (GHS), sometimes called the Purple Book, is an international system of classification of chemicals by types of hazard and propounds harmonized hazard communication elements, including labels and safety data sheets (see <http://tinyurl.com/yv8zxt>). It was developed to provide an international standard for classifying and identifying hazardous chemicals given the increasing role of global trade in these chemicals. The first edition was approved in 2002 and published in 2003, and the third revised edition was published in July 2009 and is available at <http://tinyurl.com/ye6skk3>. (Sato K, Kusaka Y, Japanese Society of Occupational and Environmental Allergy. A proposal for guideline for prevention of allergic occupational asthma in conformity with the globally harmonized system of classification and labelling of chemicals (GHS). *Industrial Health* 2007 Dec; 45(6):721-729.) -James M. Madsen, MD, MPH, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; [zmaddoc@gmail.com](mailto:zmaddoc@gmail.com)

**Friday, December 11, 2009**

**Question:**

Mercury spills into the environment (from a variety of sources) are not unusual or uncommon events. What is the legal requirement for the reporting of such environmental spills?

**Answer:**

Under U.S. Federal law, the release or spill of 1 lb (33 mL; about 2 tablespoons) or more of mercury into the environment must be reported to the federal government. The primary contact for reporting these events is the National Response Center, operated by the U.S. Coast Guard for the National Response Team established under the National Contingency Plan for Oil and Hazardous Substances Releases. (Lee R, et al. A review of events that expose children to elemental mercury in the United States. 2009, Environmental Health Perspectives 117(6): 871-878)

**Thursday, December 10, 2009****Question:**

Synephrine is an alpha-1 adrenergic agonist with some beta-3 adrenergic properties. This chemical has found its way into a number of supplement products that are variously billed as weight loss enhancers. In what products is synephrine commonly found?

**Answer:**

Synephrine is the primary alkaloid in bitter orange peel (Citrus aurantium) also known as "sour orange" or "Seville orange". Supplements may be labeled with any of these names and are often billed as "ephedra-free". Synephrine may also appear in some traditional Chinese medicines sometimes labeled as "zhi-shi" or "zhi-qiao". (Stephensen TA, Sarlay R. Ventricular fibrillation associated with use of synephrine containing dietary supplements. 2009. Military Medicine, 174(12):1313-1319.

**Wednesday, December 9, 2009****Question:**

Colchicine has been used as a successful treatment for acute gout for over 100 years but it is not without potential for severe toxicity. One example of severe toxicity may occur when colchicine is taken in conjunction with either clarithromycin or cyclosporine. Fatal toxicity has been reported when colchicine was taken in combination with these drugs. What is the mechanism for severe toxicity when colchicine is combined with these drugs?

**Answer:**

Colchicine is a substrate of CYP3A4 and the efflux transporter P-glycoprotein (P-gp). Fatal toxicity (due to excessively high levels of colchicine) has been reported in patients taking strong inhibitors of CYP 3A4 (such as clarithromycin) or strong inhibitors of P-gp such as cyclosporine. (The Medical Letter, November 30, 2009, 51(1326):93-96.

**Tuesday, December 8, 2009****Question:**

What is the measure known as LCt50 and how does the potentially lethal nerve agent sarin compare with the chemical cyanide with regard to LCt50

**Answer:**

The LCt50 represents the vapor concentration that will be lethal to 50% of the exposed population. For sarin nerve agent, the LCt50 is 100 mg X min/m<sup>3</sup> while the LCt50 for cyanide is 2500-5000 mg X min/m<sup>3</sup> (Eckstein M. Enhancing public health preparedness for a terrorist attack involving cyanide. 2008, J Emerg Med 35 (1): 59-65.

**Monday, December 7, 2009****Question:**

What is the common name of the substance that also is known by the following names: "African salad, bushmans tea, gat, miraa, qat, chat, tohai, and tschat" and what potentially abusable substance is contained in this material?

**Answer:**

Khat (Catha edulis) also known as African salad, bushmans tea, gat, kat, miraa, qat, chat, tohai, and tschat is a flowering shrub native to northeast Africa and the Arabian Peninsula. The plant usually grows from 2 to 12 feet high; however, it can reach 20 feet. Khat plants typically are grown among crops such as coffee, legumes, peaches, or papayas. Fresh khat leaves contain cathinone, a Schedule I drug under the Controlled Substances Act; however, the leaves typically begin to deteriorate after 48 hours, causing the chemical composition of the plant to break down. Once this occurs, the leaves contain cathine, a Schedule IV drug. Fresh khat leaves are glossy and crimson-brown in color, resembling withered basil. Deteriorating khat leaves are leathery and turn yellow-green in color. (Intelligence Bulletin May 2003; National Drug Intelligence Center, U.S. Dept of Justice)

**Friday, December 4, 2009****Question:**

Pepper spray, or oleoresin capsaicin (OC), is sometimes used as a self-defense agent as well as a law enforcement tool to subdue and gain control of unruly individuals. When human skin is exposed to this material, erythema and pain occurs and may persist for minutes to hours. What is the best decontamination fluid to treat skin that has come into contact with oleoresin capsaicin (OC)?

**Answer:**

A recent study compared the efficacy of five fluids that have been proposed as being efficacious to decontaminate OC skin exposures: aluminum hydroxide-magnesium hydroxide, 2% lidocaine, milk, water, and baby shampoo. This study reported no statistically significant difference in pain relief between these five fluids. The authors concluded that "copious water decontamination and, possibly oral analgesics, should remain the preferred method of pain control after topical OC exposure" (Barry JD, et al. A randomized controlled trial comparing treatment regimens for acute pain for topical oleoresin capsaicin (pepper spray) exposure in adult volunteers. 2008, Prehospital Emerg Care 12:432-437.

**Thursday, December 3, 2009****Question:**

What is Reinke's edema and what toxicological risk factor has been causally linked to the development of this disorder?

**Answer:**

Reinke's edema is also called polypoid corditis. It is characterized by swelling of the superficial lamina propria (or Reinke's layer) of the vocal cords. Clinically this disorder often occurs in middle-aged females and is characterized by a "husky" or "gravely" voice. The primary toxicological risk factor for the development of Reinke's edema is exposure to tobacco smoke. Studies have demonstrated that the clinical manifestation of this disease, in many cases, is related to the number of cigarettes smoked daily as well as the duration of exposure to tobacco smoke. It is important to note that the existence of Reinke's edema is not considered a precancerous condition. (Marcotullio D, et al. Reinke's edema and risk factors: clinical and histopathologic aspects. 2002, Am J Otolaryngology 23(2):81-84)

**Wednesday, December 2, 2009****Question:**

What is depleted uranium and what is the most common route for human exposure to this substance?

**Answer:**

Naturally occurring uranium is composed of three isotopes, U-234, U-235, and U-238. Depleted uranium (DU) is a byproduct of the enrichment of naturally occurring uranium for its most radioactive isotope, U-235. The extremely dense and pyrophoric properties of DU make it an excellent metallic substrate for radiation shielding, counterbalances, and in military armor and ammunition. It is well documented that DU can be internalized as shrapnel or inhaled from battlefield (and other) exposure sources. (Jiang GT and Aschner M. Neurotoxicity of depleted uranium. 2006. Biol Trace Elem Res, 110:1-17)

**Tuesday, December 1, 2009****Question:**

A recent CDC report focused on the use of hair testing used to attempt to link antimony contained in the textile used to make uniforms for firefighters with possible antimony "toxicity" possibly due to dermal absorption from the uniforms. As a result of the detailed analysis of this situation, the CDC has published important reminders to clinicians regarding the use of hair testing in cases that may involve heavy metals. What reminders were issued by the CDC in this regard?

**Answer:**

The reminders noted by the CDC are as follows: "The decision to perform laboratory testing for heavy metals should be based on whether symptoms are consistent with toxicity from these metals and whether a likelihood of exposure exists. Hair testing is not reliable or valid for measuring heavy metals in the body (except for methylmercury) and does not predict toxicity. Standards on methods of hair collection, storage, and analysis are lacking. No regulation or certification of laboratories conducting hair analysis exists. Different laboratories have reported different results for hair samples collected from the same person and use different reference ranges. Hair analysis cannot distinguish between internal (substances inside one's body) and external (substances that might stick to hair, such as ash or hair-care products) exposure. These limitations render hair analysis results uninterpretable. The American Medical Association and Agency for Toxic Substances and Disease Registry do not recommend using hair testing in diagnosing or guiding treatment for heavy metal toxicity. (MMWR, November 27, 2009, 58(46):1300-1302) Additional information regarding the use of hair testing in similar settings as the above scenario can be found at: [http://www.atstdr.cdc.gov/hac/hair\\_analysis/index.html](http://www.atstdr.cdc.gov/hac/hair_analysis/index.html): Agency for Toxic Substances and Disease Registry. Summary report: hair analysis panel discussion: exploring the state of the science. Atlanta, GA: US Department of Health and Human Services, Agency for Toxic Substances and Disease Registry; 2001.

**Monday, November 30, 2009**

**Question:**

What is the so-called "Red Man Syndrome"?

**Answer:**

Red Man Syndrome (RMS) is the most common adverse reaction reported associated with the administration of vancomycin. RMS is characterized by flushing of the upper body, pruritus, burning sensations and occasionally hypotension. Chest pain and muscular spasm may also occur. RMS is likely related to the release of histamine and/ or the rate of drug infusion. The incidence rate for RMS is reportedly as high as 50%. Antihistamines may ameliorate the reaction. Other drugs including ciprofloxacin, amphotericin B, rifampicin and teicoplanin may also be associated with a similar "red man syndrome". (Sivagnanam S, Deleu D. Red man syndrome. 2003 Crit Care, 7(2):119-120)

**Friday, November 27, 2009**

**Question:**

Methadone is a synthetic opioid associated with prolonged Q-T intervals and torsades de pointes. What other opioid or opioid-related compounds have been associated with adverse effects on Q-T intervals when used at therapeutic levels?

**Answer:**

Methadone and Levocetylmethadol (LAAM or Orlaam) are the only opioid or opioid-related compounds that have, to date, been associated with adverse effects on the Q-T interval when used at therapeutic levels. (Stringer J, et al. (2009) Methadone associated Q-T interval prolongation and torsades de pointes. Am J Health Sys-Pharm,66:825-833)

**Wednesday, November 25, 2009**

**Question:**

The ingestion of so-called button batteries in children (or others) is a potentially serious problem based on the fact that these objects may lodge in the esophagus. When these objects do lodge in the esophagus, serious esophageal injury and even death may occur. What are the four usual mechanisms of injury that may be at play when these batteries lodge in the esophagus?

**Answer:**

The four potential mechanisms of harm in this setting are: 1. Toxic effects due to systemic absorption of chemicals contained within the battery. (e.g. Most of the mercuric oxide in batteries changes into nontoxic substances after ingestion, however some batteries may contain as much as 5 grams of mercuric oxide, potentially a lethal dose. Batteries containing lithium, manganese, and heavy metals other than mercury do not usually cause toxicity from systemic absorption of those metals) 2. Electrical discharge and mucosal burn. (e.g. Animal experiments have shown that it is not necessary for the battery to leak alkali to cause mucosal damage. A battery in the lumen of the esophageal can complete a local electrolytic circuit and thus cause local damage) 3. Necrosis due to direct pressure (e.g. As is possible with virtually any other foreign body). 4. Caustic injury due to leakage. (e.g. Some batteries may demonstrate instantaneous release of battery contents when the battery is immersed in a saline environment and local damage may occur by direct effects on the local mucosa) (Yardeni D, et al. Severe esophageal damage due to button battery ingestion: can it be prevented? 2004, Pediatric Surg Int 20:496-501.

**Tuesday, November 24, 2009**

**Question:**

With regard to the illicit production of methamphetamine, what does the term "smurfing" refer to?

**Answer:**

Smurfing is a method used by some methamphetamine traffickers to acquire large quantities of precursor chemicals to be used in methamphetamine production. Methamphetamine producers purchase chemicals in quantities at or below the threshold for multiple retail locations. Illegal methamphetamine producers often enlist the assistance of several friends or associates to increase the speed of their smurfing operations and the quantity of chemicals acquired. (National Methamphetamine Threat Assessment. National Drug Intelligence Center, U.S. Department of Justice, December, 2008)

**Monday, November 23, 2009**

**Question:**

"Asbestos" is the general industrial term encompassing six (6) different naturally occurring fibrous silicates. Name these six different fibrous silicates and the general mineral group classification to which they each belong.

**Answer:**

Amosite, crocidolite, tremolite, anthophyllite and actinolite all belong to the amphibole mineral group, while chrysotile is a member of the so-called serpentine group. (Fubini B and Fenoglio I,(2007) Toxic potential of mineral dusts. Elements, 3:407-414)

**Friday, November 20, 2009**

**Question:**

During the 1920's and 1930's an epidemic of poisoning due to consumption of beverages contaminated with the chemical tri-ortho cresyl phosphate (TOCP) swept across the United States. Many individuals who drank beverages containing TOCP developed a neuromuscular disorder that came to be known colloquially as the "Jake Leg". How many Americans are estimated to have been so afflicted across the U.S. during that era?

**Answer:**

Estimates place the number of afflicted persons in the range of 35,000 individuals. (Baum D. "Jake Leg. How the blues diagnosed a medical mystery". The New Yorker, September 15, 2003: 50-57)

**Thursday, November 19, 2009**

**Question:**

Diethylene glycol (DEG) has been the culprit chemical in a number of mass poisonings in the past when substituted as a diluent in pharmaceutical preparations. What consumer products may contain DEG

**Answer:**

DEG is commonly used as a solvent and ingredient in numerous consumer products, including Sterno®, antifreeze preparations, wallpaper strippers, automotive chemicals (e.g., brake fluids), and in artificial fog solutions. (Marraffa J.M, et al. (2008) Diethylene glycol: widely used solvent presents serious poisoning potential. J Emerg Med., 35(4): 401-406)

**Tuesday, November 17, 2009**

**Question:**

Perchlorate salts have been used as pharmaceuticals, in propellants for rockets and missiles, in explosives, fireworks, safety flares and air bag inflation systems. Since 1997, perchlorates have been found in drinking water supplies throughout the United States. Perchlorates act as competitive inhibitors of iodine uptake by the thyroid via a sodium-iodide symporter. What is the effect on thyroid function of ingestion of low doses of perchlorates over time?

**Answer:**

One admittedly small study that looked at a 6-month exposure to perchlorate at doses up to 3 mg/d had no effect on thyroid function. These results suggest that healthy, euthyroid individuals, with normal levels of iodine intake, can tolerate chronic exposure to perchlorate at doses up to 3 mg/d without any effects on thyroid function, including inhibition of iodide uptake. (Braverman LE, et al. Effects of six months of daily low dose perchlorate exposure on the thyroid function in healthy volunteers. 2006, J Clin Endocrinology and Metabolism, 91(7): 2721-2724.

**Monday, November 16, 2009**

**Question:**

Methylene chloride (dichloromethane) is an industrial chemical that is metabolized to carbon monoxide in the human body and consequently elevated carboxyhemoglobin levels may result. How high can carboxyhemoglobin levels range as a result of exposure to methylene chloride?

**Answer:**

While only about 1/3 of inhaled methylene chloride is metabolized to carbon monoxide in the human liver, carboxyhemoglobin levels ranging as high as 30-50% have been reported following human exposure to methylene chloride. (Raphael M, et al. Acute methylene chloride intoxication- a case report on domestic poisoning. 2002, Eur J Emerg Med, 9:57-59)

**Friday, November 13, 2009**



**Question:**

Long-term, subacute exposure to carbon monoxide differs from acute carbon monoxide poisoning in many respects. What are the clinical features and problems that have been reported to be associated with long-term, subacute carbon monoxide exposure?

**Answer:**

The clinical scenario consistent with long-term, subacute carbon monoxide exposure involves exposures that are greater than 24 hours in duration and generally intermittent over the course of weeks to years. Symptoms and findings reportedly may include chronic fatigue, affective conditions and emotional distress, memory problems, difficulty working, sleep disturbances, vertigo, neuropathy, parasthesias, recurrent infections, polycythemia, abdominal pain, and diarrhea. (Weaver L. Carbon monoxide poisoning. New England Journal of Medicine. 2009;360(12):1217-25.) Susan Ney Miller, MD, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; contact at smiller01@drexelmed.edu.

**Thursday, November 12, 2009**

**Question:**

With the current fears of H1N1 flu, the use of ethanol-based hand sanitizers has increased in popularity. Is it possible for a person to elevate their blood alcohol level with the use of these products?

**Answer:**

No. A study of 5 healthy male volunteers who used 5 mL of 63% ethanol-based hand sanitizer 50 times over 4 hours did not demonstrate an elevation of blood alcohol level. This study did not look at misuse of the product and certainly inappropriate ingestion of this material could result in measurable levels of blood ethanol. (Miller M, et al. Does the clinical use of ethanol-based hand sanitizers elevate blood alcohol levels? A prospective study. American Journal of Emergency Medicine. 2006;24:815-7) Susan Ney Miller, MD, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; contact at smiller01@drexelmed.edu.

**Wednesday, November 11, 2009**

**Question:**

Propofol infusion syndrome is a rare but potentially lethal complication of prolonged propofol infusions. What signs and symptoms, including laboratory findings, may lead a clinician to believe a patient is developing the propofol infusion syndrome?

**Answer:**

Propofol infusion syndrome may include some (or several) of the following features: hypotension, metabolic acidosis, lactic acidosis, hyperkalemia, hyperlipidemia, rhabdomyolysis with or without myoglobinuria, acute renal failure, hepatomegaly with hepatic steatosis, cardiac arrhythmias, and heart failure. Sinus tachycardia may be the first clinical sign, however ST-elevation in the right precordial leads may be the first sign of cardiac instability. Increasing hyperlipidemia may be an early laboratory finding. Cardiac failure and multi-organ failure are late signs. The development of unexplained signs/symptoms as above, in the critically ill patient receiving propofol, should prompt discontinuation of propofol in most cases and consideration of substituting a different agent(s) for sedation. (Orsini, J, et al. Propofol infusion syndrome: Case report and literature review. American Journal of Health-System Pharmacy. 2009;66:908-915.) Susan Ney Miller, MD, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; contact at smiller01@drexelmed.edu.

**Tuesday, November 10, 2009**

**Question:**

Thimerosal has been used as a preservative in vaccines and considerable controversy has surrounded the use of this substances with regard to the association that some believe may exist between thimerosal and an increased risk for autism in vaccinated children. What is the active ingredient in thimerosal?

**Answer:**

Ethyl mercury is the active ingredient in thimerosal. While METHYL mercury blood levels have been shown to be helpful in predicting toxicity, the importance of blood levels for ETHYL mercury is not clear. The cited study reports low levels of mercury in premature and low birth weight newborn infants after receiving thimerosal-containing vaccines and the authors suggest a low risk for toxicity from this exposure (Pichichero ME, et al. Mercury levels in premature and low birth weight newborn infants after receipt of thimerosal-containing vaccines. 2009, J Pediatrics; 155:495-499)

**Friday, November 6, 2009**

**Question:**

What is currently considered the chelator of choice in the treatment of polonium-210 poisoning (internal contamination)?

**Answer:**

The currently recommended chelator of choice to treat polonium-210 poisoning (internal contamination) is dimercaprol as per the National Council on Radiation Protection and Measurements. This group also currently recommends penicillamine as an alternative. There is some discussion however regarding the best agent, all things considered, and parenteral DMPS or oral DMSA has also been suggested to treat polonium-210 poisoning. Research in this area will, hopefully, be forthcoming and it may be that a combination of chelators will eventually be identified as the most efficacious treatment in this setting. (Jefferson, RD, et. al. Diagnosis and treatment of polonium poisoning. 2009, Clin Tox, 47:379-392.)

**Thursday, November 5, 2009**

**Question:**

Styrene is an aromatic solvent classified as an alkylbenzene. Occupational exposure to styrene occurs primarily in the manufacturing of fiberglass-reinforced plastics and composites. Since 1988, nine studies have been published on the relationship between occupational exposure to styrene and what specific toxicity

**Answer:**

These studies addressed hearing loss as a possible toxicity for occupational exposure to styrene. Since 1988, nine studies have been published on the relationship between occupational exposure to styrene and hearing loss. These reports included more than 1000 workers exposed to styrene, both with and without concurrent noise exposure. Exposure assessment was usually based on styrene measurements in the breathing zone during several hours of one working day. Some of the studies also used biological monitoring of styrene exposure based on determination of its urinary metabolites. Of the nine studies, seven show some effects on the auditory system that were associated with styrene-alone exposure. (Johnson AC. Relationship between styrene exposure and hearing loss: a review of human studies. International Journal of Occupational Medicine & Environmental Health. 20(4):315-25, 2007)

**Wednesday, November 4, 2009**

**Question:**

What forensic-toxicology findings are specific for death from inhalation of nitrogen gas?

**Answer:**

Nitrogen can cause death as a simply asphyxiant, by displacing oxygen. Because nitrogen is a normal component of the blood, forensic analysis of biological samples in autopsies of victims cannot be used to establish nitrogen as the cause of death. Determination of death in cases in which nitrogen is suspected to be the causative agent depends upon investigation of the scene and of the circumstances surrounding the death. (Harding BE, Wolf BC. Case report of suicide by inhalation of nitrogen gas. American Journal of Forensic Medicine and Pathology 2008 Sep; 29(3):235-237.) James M. Madsen, MD, MPH, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA

**Tuesday, November 3, 2009**

**Question:**

What chemical was responsible for the deaths of thousands of sheep in Utah in 1968?

**Answer:**

One or more nerve agents, including VX, were released over Skull Valley, Utah in 1968 after a spray valve failed to close after an aerial test. VX is a particularly potent nerve agent that is a liquid at usual temperatures. (Rabinowitz P, Wiley J, Odofin L, Wilcox M, Dein FJ. Animals as sentinels of chemical terrorism agents: An evidence-based review. Clinical Toxicology 2008; 46(2):93-100.) James M. Madsen, MD, MPH, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; zmaddoc@gmail.com

**Monday, November 2, 2009**

**Question:**

Spanish fly has been used historically (and hopefully) by some as an aphrodisiac. Its purported sexually enhancing effects are based on its ability to cause urinary-tract irritation with genital swelling and, in some cases, priapism. What is the active ingredient of Spanish fly and what is its potential toxicity following ingestion?

**Answer:**

Spanish fly is a powder obtained from grinding up dead blister beetles (*Cantharis vesicatoria*). Its active ingredient is cantharidin, which is secreted by other blister beetle species as well. In addition to its use as a purported aphrodisiac, cantharidin has also been used as a wart remover. Skin contact with cantharidin from male blister beetles can cause painful blisters. Ingestion of as little as 10 mg of pure cantharidin may reportedly cause death in an adult human. It is thought that cantharidin inhibits protein phosphatases Types 1 and 2A, increasing capillary permeability of albumin and leading to diffuse endothelial injury with consequent edema, inflammation, vesication, and, after ingestion, gastrointestinal hemorrhage and hematuria. (Tagwireyi D, et al. Cantharidin poisoning due to blister beetle ingestion. *Toxicol* 2000 Dec 1; 38(12):1865-1869.) James M. Madsen, MD, MPH, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; zmaddoc@gmail.com

**Friday, October 30, 2009****Question:**

Metal fume fever (MFF) is an occupational disorder usually associated with welding, galvanizing and smelting activities. The clinical manifestations of MFF are usually described as similar to a flu like illness with variable symptoms including fever, headache, fatigue, malaise, arthralgias and myalgias as well as respiratory complaints. The most common metal sources for MFF are zinc and copper however a number of other metal oxides have reported to be associated with a MFF syndrome. What are the metals that have been associated with the development of MFF?

**Answer:**

The following metals (usually the oxides thereof) have been associated with the development of MFF: Zinc, copper, magnesium, iron, chromium, cadmium, nickel, manganese, mercury, cobalt, lead, antimony, selenium, beryllium, vanadium, silver, aluminum, and titanium. (Otani N, et al. Acute group poisoning by titanium dioxide: inhalation exposure may cause metal fume fever. 2008, *Am J Emerg Med*, 26: 608-611)

**Thursday, October 29, 2009****Question:**

Paclitaxel in combination with carboplatin is currently considered to be first line chemotherapy for advanced ovarian cancer. Patients typically receive these drugs every three weeks. What organ system toxicity is of greatest concern in patients receiving the chemotherapy combination of paclitaxel and carboplatin?

**Answer:**

Neurotoxicity is the adverse reaction of greatest concern in patients receiving this combination of drugs with parenthesis being the usual dose limiting toxicity. (Katsumata N, et al. Dose-dense paclitaxel once a week in combination with carboplatin every three weeks for advanced ovarian cancer. 2009, *The Lancet*, 374:1331-1338)

**Wednesday, October 28, 2009****Question:**

Based on the current influenza and H1N1 hysteria there will be a large number of prescriptions filled for oseltamivir in the coming weeks. What are the potential adverse effects associated with oseltamivir (Tamiflu)?

**Answer:**

Oseltamivir is a pro drug that is readily absorbed in the GI tract and converted by hepatic carboxylesterases to a single active metabolite, oseltamivir carboxylate. Transient nausea and vomiting are the only adverse events consistently reported more frequently by subjects taking oseltamivir when compared with placebo recipients. There is no convincing evidence at present that oseltamivir is associated with cardiac toxicity including QTc prolongation. In addition, there are no convincing studies that reveal evidence of adverse CNS events including seizures or psychiatric effects. (Dutkowski R, et al. Safety and pharmacology of oseltamivir in clinical use. 2003, *Drug Safety*, 26(11):787-801) The manufacturer of Tamiflu (oseltamivir) does point out that: Rare but serious skin reactions and allergic reactions have been reported. Stop taking Tamiflu and call your doctor if you experience any of these reactions, as they could be very serious. People with the flu, particularly children and adolescents, may be at an increased risk of self-injury and confusion shortly after taking Tamiflu and should be closely monitored for signs of unusual behavior. A healthcare professional should be contacted immediately if the patient taking Tamiflu shows any signs of unusual behavior. They also point out: The concurrent use of Tamiflu and live attenuated influenza vaccine (LAIV) intranasal has not been evaluated. However, due to the possibility for interference between these products, LAIV should not be given within 2 weeks before or 48 hours after taking TAMIFLU, unless it is deemed appropriate by your doctor.

**Tuesday, October 27, 2009****Question:**

What are the three groups of drugs that may predispose to the development of lithium toxicity in patients (especially the elderly) also taking lithium and what is the probable mechanism for lithium toxicity in these cases?

**Answer:**

The three groups of drugs that tend to predispose to the development of lithium toxicity in patients also taking lithium are 1- diuretics that promote renal sodium wasting, via enhancement of tubular reabsorption of lithium, 2-ACE inhibitors, via enhancement of tubular reabsorption of lithium, and 3- NSAIDs via interference with renal prostaglandin synthesis. (Juurlink DN, et al. Drug-induced lithium toxicity in the elderly: A population-based study. 2004, *J Am Geriatr Soc*, 52:794-798, 2004)

**Monday, October 26, 2009****Question:**

Chromium (Cr) exists in several valence states including the +6, +3 and 0 oxidative forms. Occupational exposure to what oxidative form of Cr has been associated with the development of pulmonary cancers?

**Answer:**

Occupational exposure to Cr (VI) compounds, but not to other oxidative forms of Cr, has been widely reported as being a cause for pulmonary cancers. (Salnikow K, Zhitkovich A. Genetic and epigenetic mechanisms in metal carcinogenesis and cocarcinogenesis: Nickel, arsenic, and chromium. 2008, *Chem Res Toxicol*, 21:28-44)

**Friday, October 23, 2009****Question:**

What is argyria and what substances have been reported in the literature to cause argyria?

**Answer:**

Argyria is a benign skin condition characterized by a bluish-gray discoloration of the skin. It can be generalized or localized and it is caused by the cutaneous deposition of silver granules in the skin as a result of exposure to, or ingestion of, silver containing materials. Reported causes for generalized argyria include the following: exposure to silver containing nose drops, silver-containing eye drops, colloidal silver drinks, silver containing breath freshener, silver pills, silver coated sugar particles and photographic film as well as ingested or topical silver nitrate. Localized argyria has been reported in associations with silver earrings, topical silver nitrate, silver sulfadiazine topical cream, and acupuncture needles. There is no known treatment for argyria and the skin discoloration is, in most cases, permanent. (Brandt D, et al. Argyria secondary to ingestion of homemade silver solution. 2005, *J Am Acad Dermatol*, 53:S105-S107)

**Thursday, October 22, 2009****Question:**

Which bio-markers have been commonly used to assess for renal injury in the face of occupational cadmium exposure?

**Answer:**

The urinary excretion of certain protein bio-markers has been used to assess the potential for renal injury in occupational exposure to cadmium. These biomarkers include albumin, beta-2 microglobulin, retinol binding protein, and NAG (N-acetyl-glucosaminidase). (Fowler BA. Monitoring of human populations for early markers of cadmium toxicity: A review. 2009, *Toxicology and Applied Pharmacology*, 238:294-300)

**Wednesday, October 21, 2009****Question:**

An industrial accident occurred in the town of Seveso, Italy, in 1976 and exposed a large population to substantial amounts of what toxicant?

**Answer:**

2,3,7,8-tetrachlorodibenzo-p-dioxin, also known as TCDD or dioxin was the toxicant released as a result of the infamous accident at Seveso, Italy, in 1976. (Bertazzi, P, et al. The Seveso studies on early and long term effects of dioxin exposure: A review. 1998, *Env Health Perspectives*, 106:627-633.

**Tuesday, October 20, 2009**

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**Question:**

What is hypersensitivity pneumonitis (HP)? What are some of the exposures that are addressed in the literature as causing HP related disorders?

**Answer:**

Hypersensitivity pneumonitis (HP) is also known as extrinsic allergic alveolitis. HP is an inflammatory disorder of the lung parenchyma and bronchioles caused by repeated inhalations of airborne environmental antigens to which an individual has been sensitized by previous exposures. The diagnosis of HP can be challenging due to a high variability in clinical presentations and disease progression in various individuals. Some (there are many) commonly discussed exposures and their associated antigens and diseases are listed as follows: Moldy hay: antigen/Faeni rectivirgula; disease/"Farmer's lung" Pigeons: antigen/serum-feathers-droppings; disease/"Pigeon breeders lung" Parakeets: antigen/serum-feathers-droppings;disease/"Budgerigar fanciers lung" Hot tubs: antigen/Mycobacterium avium complex; disease/"Hot tub lung" Metalworking fluids: antigen/Mycobacterium sp.; disease/ hypersensitivity pneumonitis (Madison JM. Hypersensitivity pneumonitis. 2008; Arch Pathol Lab Med. 132:195-198)

**Monday, October 19, 2009**

**Question:**

Occupational exposure to what toxicant has been causally associated with the development of angiosarcoma of the liver?

**Answer:**

Prolonged occupational exposure to high doses of vinyl chloride (NOT polyvinyl chloride/PVC) has been causally associated with the development of angiosarcoma of the liver. (Bosetti C, et al Occupational exposure to vinyl chloride and cancer risk: a review of the epidemiologic literature. 2003, Eur J Cancer Prevention, 12:427-430.)

**Friday, October 16, 2009**

**Question:**

Intralipid 20%, is a lipid emulsion substance approved by the FDA as a source for calories and fatty acids for patients requiring parenteral nutrition. Over the past few years, Intralipid has gained quite a bit of attention as a potential agent to treat certain life threatening drug toxicities. What are the constituents of Intralipid 20%?

**Answer:**

Intralipid 20% is comprised of 20% soybean oil (Intralipid 10% contains 10% soybean oil), 1.2 % egg yolk phospholipids, 2.25% glycerin and water for injection (Corman S, Skledar S. Use of lipid emulsion to reverse local anesthetic-induced toxicity. 2007, Anns Pharmacotherapy, 41:1873-1877

**Thursday, October 15, 2009**

**Question:**

Hydrofluoric acid is a weak organic acid that is used for a variety of applications including glass etching, oil refining, and rust removal, among other uses. What is the typical concentration of HF in household products? In industrial products?

**Answer:**

The concentration of HF in household products is typically less than 10% while the concentration in industrial products may be as high as 70%. (Vohra R, et al. Recurrent life threatening ventricular dysrhythmias associated with acute hydrofluoric acid ingestion: Observations in one case and implications for mechanism of toxicity. 2008. Clin Tox 46:79-84.

**Wednesday, October 14, 2009**

**Question:**

What herbal is used by some to treat anxiety, stress, ADHD, headaches, epilepsy, respiratory tract infections, and urinary infections, and is thought to act via GABA receptors?

**Answer:**

Kava kava is the popular herbal remedy described above. In 2002 the FDA issue a warning regarding this herbal and discussed possibly severe liver toxicity that might be associated with the use of kava-containing products. In 2003,kava extracts were banned in Canada and the European Union. Nonetheless kava containing products are readily available from a variety of internet web sites. (Tovar R, Petzel R. Herbal Toxicity. 2009, Disease-a-Month, 55(10):587-642)

**Tuesday, October 13, 2009**

**Question:**

Clozapine is known to induce GI hypo-motility. In some cases this may even lead to the development of toxic megacolon. GI hypomotility due to clozapine reportedly occurs with an estimated prevalence of 0.3% and a very high mortality rate in the range of 27-28%. What are the risk factors for the development of clozapine-induced GI hypo-motility?

**Answer:**

Risk factors for GI hypo-motility related to clozapine use include high clozapine doses, acute increases in serum clozapine levels due to such factors as medical illness, fever or co-administration of the cytochrome P-450 inhibitors fluoxetine or fluvoxamine, concomitant use of anti-cholinergic medications, history of GI disease and bowel surgery. (Alam H, Fricchione GL, et al. Case 31-2009: A 26 year old man with abdominal distention and shock. (2009) NEJM, 361(15): 1487-1496.

**Monday, October 12, 2009**

**Question:**

Diphenhydramine has recently been reported to cause opsoclonus, which refers to involuntary, nonrhythmic, darting oscillations (often with both vertical and horizontal components, sometimes seen sequentially and sometimes combined to form a looping motion) of the eyes. Besides diphenhydramine, what can cause opsoclonus?

**Answer:**

Opsoclonus is seen most commonly in viral or paraneoplastic encephalitis but has also been reported in patients exposed to lithium or to organophosphorous compounds. (Irioka T, Yamanami A, Uchida N, Iwase M, Yasuhara H, Mizusawa H. Opsoclonus caused by diphenhydramine self-poisoning. Journal of Neuro-Ophthalmology 2009 Mar; 29(1):72-73.) James M. Madsen, MD, MPH, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA. (zmaddoc@gmail.com)

**Thursday, October 8, 2009**

**Question:**

A patient presents with shortness of breath and decreased level of unconsciousness after an unknown ingestion. The patient is intubated for airway protection. Upon urinary catheterization to evaluate urinary output, the nurse reports that his urine is black. What is the toxicological differential diagnosis of black urine?

**Answer:**

Medications that may cause black urine include L-dopa, methyl dopa, chloroquine, primaquine, furazolidone, metronidazole, nitrofurantoin, cascara/senna laxatives, methocarbamol, and sorbitol. In this case, the ingestant was actually cresol, a household disinfectant. Medical causes of black (or at least very dark) urine include hemoglobinuria, myoglobinuria, alkaptonuria, melanuria, porphyrinuria, and tyrosinuria. (Liu, SW, et al. A man with black urine. Annals of Emergency Medicine. 2009;53:836.) Susan Ney Miller, MD, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; contact at smiller01@drexelmed.edu.

**Wednesday, October 7, 2009**

**Question:**

Modafinil (Provigil) is a non-amphetamine stimulant sometimes used in the treatment of narcolepsy, sleep apnea, and shift work sleep disturbances. What are the major signs of toxicity following overdose with this agent?

**Answer:**

Tachycardia, insomnia, agitation, dizziness, and increased anxiety are the most commonly reported signs and symptoms associated with modafinil toxicity in overdose. (Spiller, HA, et al. Toxicity from modafinil ingestion. Clinical Toxicology, 2009;47(2):153-156.) Susan Ney Miller, MD, Fellow in Medical Toxicology, Drexel University College of Medicine, Philadelphia, PA; contact at smiller01@drexelmed.edu.

**Tuesday, October 6, 2009**

**Question:**

Dimercaptosuccinic acid (DMSA) has been used in the treatment of lead poisoning since the mid-1960's. What is the most common adverse effect of DMSA therapy?

**Answer:**

Mild elevation of hepatic transaminase activity is the most common adverse effect of DMSA therapy. However, it is important to note that this has not been associated with clinically important liver toxicity and the transaminase elevation generally resolves when DMSA is discontinued. (Bradberry S, Vale A., 2009, Dimercaptosuccinic acid (DMSA) in inorganic lead poisoning. Clin Tox 47(7):617-631)



**Monday, October 5, 2009****Question:**

What would be your primary suspicion in a case of a youngster who ingested an unknown purple powder and presents with drooling, lip swelling, edema of the tongue, and black staining of the tongue, gingivae, teeth, and oral mucosa?

**Answer:**

The exact identity of the compound should of course be determined if possible, but there are enough clues here to suggest contact with a corrosive substance. In such cases, abdominal pain may not necessarily be present even with corrosive damage to the esophagus and stomach, but the presence of drooling is an indication for esophagogastrosocopy. In this case, the purple substance was potassium permanganate; and bronchoscopy and esophagogastrroduodenoscopy showed staining in the posterior pharynx, esophagus, and tracheobronchial tree along with mild supraglottic edema. He did not require intubation and was discharged after two days of observation. (McKeown NJ, Horowitz BZ. From Russia with love--ingestion of a purple powder. Pediatric Emergency Care 2009 Jun; 5(6):423-425.) James M. Madsen, MD, MPH, Fellow in Medical Toxicology, Drexel Univ College of Medicine, Philadelphia, PA

**Wednesday, September 30, 2009****Question:**

What is liposomal lidocaine?

**Answer:**

Liposomes are microscopic, spherical, phospholipid- based carriers that can facilitate and enhance the penetration of certain drugs thru the skin. Lidocaine can be encapsulated in a liposomal structure to form liposomal lidocaine. It has been suggested that liposome-encapsulated lidocaine is at least as efficacious as other topical anesthetics such as EMLA. (Eidelman A, et al., Anns Emerg Med. 2005

**Tuesday, September 29, 2009****Question:**

Patients suffering from hemolytic anemia may manifest an increase in carboxyhemoglobin levels. What COHgb levels are consistent with this potential increase?

**Answer:**

In hemolytic anemias the COHgb may increase to 3-4%. ( Kao LW and NanÜagas. Emerg Med Clin N Am 22 (2004) 9851018)

**Monday, September 28, 2009****Question:**

Can a fever in a patient using transdermal fentanyl cause an increase in fentanyl serum concentrations?

**Answer:**

Based on a pharmacokinetic model referenced in the product labeling materials, an increase in body temperature to 40 degrees C (104 degrees F) could increase fentanyl serum concentrations. However, no reports of clinical overdose caused by fever have been published to date. (The Medical Letter, 51(1319):64, August 24,2009

**Friday, September 18, 2009****Question:**

The FDA recently ordered the manufacturers of which two drugs used for smoking cessation to add a boxed warning regarding their risk of psychiatric symptoms and suicide?

**Answer:**

These new warnings are based on reports of a temporal relationship between the use of varenicline (Chantix) or bupropion (Zyban and others) and suicidal ideation or behavior (The Medical Letter, 51(1319):61, August 24,2009

**Thursday, September 17, 2009****Question:**

Pain is present in more than 90% of the bites from pit vipers in the United States. What is the exception?

**Answer:**

Bites from the Mojave rattlesnake (*Crotalus scutulatus*) often cause little to no pain. (Emergency Clinics of North America, 2004, 22:423-44)

**Wednesday, September 16, 2009****Question:**

How effective is Crotalidae polyvalent immune Fab (ovine) antivenom (CroFab; FabAV) in copperhead envenomations?

**Answer:**

The new ovine antivenom was not made using the venom from copperhead snakes, and patients bitten by copperheads (37% of all venomous snakebite cases in the U.S. in 2001) were not included in the clinical trials of the antivenom. A study by Lavonas et al. published in 2004 reported a rapid initial response (cessation of the progression of tissue swelling) in 88% of copperhead-envenomated patients given FabAV (the median dose was 4 vials). However, recurrent swelling occurred in 19% of cases, and one patient developed late-onset coagulopathy. As an editorial in the same journal issue points out, no relationship between swelling and tissue injury has been demonstrated for Crotaline snakebites. Moreover, neither time to return to work nor long-term limb disability was assessed in the original study. The risks of ovine-derived Fab antivenom administration are relatively low, but its cost-benefit ratio has yet to be determined for victims of copperhead bites. (Annals of Emergency Medicine, 2004 Feb, 43(2):200-206 [article] and 207-208 [editorial])

**Tuesday, September 15, 2009****Question:**

What long-term effects have been seen from copperhead bites?

**Answer:**

In one case series of 178 cases, 18 patients (10%) reported limb dysfunction manifested by persistent or recurrent edema, pain, and paresthesias. The median duration of these effects was 42 days, with a range of five to 365 days. (Journal of Toxicology: Clinical Toxicology, 2003, 41(1):29-35)

**Thursday, July 9, 2009****Question:**

*Tricholoma equestre*, also called *Tricholoma flavovirans* and yellow trich, is a species of mushroom known for its ability to cause rhabdomyolysis. Have any other mushroom species been associated with rhabdomyolysis?

**Answer:**

*Russula* species (especially *Russula subnigricans*, or blackening russula), *Boletus edulis* (king boletus), *Leccinium versipelle* (brown birch boletus), *Albatrellus ovinus* (sheep polypore), and even *Cantharellus cibarius* (chanterelle), have also been shown capable of significantly increasing creatine kinase activity, although most of these species even when consumed in large quantities produce only mild to moderate toxicity and no histopathological changes in muscle or liver. *Russula subnigricans*, however, has caused fatal rhabdomyolysis. (Experimental Biology and Medicine, 2006, 231:221-228)

**Wednesday, July 8, 2009****Question:**

What is erythromelalgia, and what substances can cause it?

**Answer:**

Erythromelalgia is a painful inflammatory condition in which intense, burning pain is felt in the hands and the feet, which may also become erythematous and swollen. It is often exacerbated by heat and relieved by cold. Transient erythromelalgia, characterized histologically by perivascular mononuclear infiltrates and prominent perivascular dermal edema without vasculitis, has been reported after oral administration of bromocriptine, verapamil, and nifedipine. Erythromelalgia resolving spontaneously after eight days to nine months has been reported following the consumption of mushrooms, including *Clitocybe acromelalga* and *Clitocybe amoenoletus*. Acromelic acids A-E have been identified as the toxic components of *Clitocybe acromelalga*. (Toxicological Reviews, 2006, 25(3):199-209)

**Tuesday, July 7, 2009**

**Question:**

In the United Kingdom, dermatitis and blistering are more frequently reported from police use of CS (2-chlorobenzylidene malononitrile) than from the use of CS-containing personal sprays. Differing circumstances of use may account for part of this difference, but is there a possible toxicological reason for the higher incidence of adverse reactions with the police preparation?

**Answer:**

The CS formulation used by police in the United Kingdom differs from the formulation used in personal protection sprays in that CS in the police formulation (but not in personal sprays) is dissolved in the solvent methylisobutylketone (MiBK). MiBK when sprayed directly onto the skin and into the eyes can result in local irritation and pain as well as dizziness, headache, drowsiness, weakness, and loss of appetite. MiBK may also prolong the actions of CS. (Emerg Med J, 2004 September, 21(5): 548?552)

**Monday, July 6, 2009**

**Question:**

What ocular effects, in addition to local irritation, can occur following the use of the riot-control agent CS (2-chlorobenzylidene malononitrile)?

**Answer:**

CS, delivered as a spray, a smoke, or as small particles forcibly ejected from CS ?grenades,? can cause intense lacrimation, blepharospasm, conjunctival injection, and periorbital edema. Because riot-control agents are popularly called ?tear gas,? it is easy to overlook the additional complications of particulate CS (which is a solid) ejected at close range from CS canisters. Such exposure can lead to impaction of particles onto the surface of eye with resulting conjunctival tearing, corneal edema, secondary glaucoma, cataracts, hyphema, vitreous hemorrhage, and traumatic optic neuropathy. (Journal of Trauma-Injury Infection & Critical Care, 2002 Mar, 52(3):595-600)

**Friday, June 26, 2009**

**Question:**

Name the anti-neoplastic agents that have been most commonly implicated as potentially causing toxic leukoencephalopathy.

**Answer:**

Methotrexate and carmustine are most commonly implicated as causing toxic leukoencephalopathy. Numerous other agents have also been described, including cisplatin, cytarabine, fluorouracil, levamisole, fludarabine, thiotepa, interleukin-2, and interferon-alpha. (Filley CM. Kleinschmidt-DeMasters BK. Toxic Encephalopathy. New England Journal of Medicine. 2001;345(6):425-32)

**Thursday, June 25, 2009**

**Question:**

Describe the potential adverse clinical effects related to phenylpropanolamine (PPA) use.

**Answer:**

Phenylpropanolamine, a formerly popular over-the-counter sympathomimetic amine, was often used as a dieting agent, as well as for cough and cold symptoms. It has been reported to cause numerous adverse effects, particularly in young female adults, including myocardial infarction, hemorrhagic stroke, and hypertension. Pilsczek FH. Karcic AA. Freeman I. Case report: Dexatrim (Phenylpropanolamine) as a cause of myocardial infarction. Heart & Lung. 32(2):100-4, 2003 Mar-Apr.

**Wednesday, June 24, 2009**

**Question:**

What is naringin, and what effects does it have upon the body?

**Answer:**

Naringin is an active ingredient of grapefruit juice that is metabolized by gut flora to the flavanone naringenin, a potent CYP inhibitor. Specifically, it has been shown to inhibit activity of CYP1A2, CYP3A4, and CYP19. Moon YJ. Wang X. Morris ME. Dietary flavonoids: effects on xenobiotic and carcinogen metabolism. Toxicology in Vitro. 20(2):187-210, 2006 Mar.

**Tuesday, June 23, 2009**

**Question:**

What is the toxicological significance of 2,5-hexanedione?

**Answer:**

2,5-hexanedione is a potentially harmful metabolite of both n-hexane and methyl n-butyl ketone. It is believed to be the agent responsible for producing neurotoxicity leading to peripheral neuropathy in some individuals who may have suffered chronic exposures to these chemicals. (Dick FD. Solvent neurotoxicity. Occup Environ Med. 2006;63:221-26)

**Monday, June 22, 2009**

**Question:**

Describe the pattern of pathology exhibited on neuroimaging in patients with chronic toluene abuse.

**Answer:**

A recent review of this topic found that toluene preferentially affects periventricular and subcortical (e.g. basal ganglia, thalamus) regions, as well as white matter structures. White matter changes were characterized by demyelination, hyperintensities, callosal thinning, and loss of gray matter-white matter boundaries. (Yucel M et al. Toluene misuse and long-term harms: a systematic review of the neuropsychological and neuroimaging literature. Neuroscience and Biobehavioral Reviews. 2008;32:910-26)

**Friday, June 19, 2009**

**Question:**

What is BZ? Describe this agent and its mechanism of action.

**Answer:**

BZ is the NATO designation for 3-quinuclidinyl benzilate, or QNB, which was once weaponized by the U.S. as a chemical-warfare incapacitating agent. It is a white solid that can be dispersed as a dust or dissolved in organic solvents to form a solution. As a glycolate anticholinergic agent, it acts as a competitive inhibitor of acetylcholine at muscarinic receptors and produces an anticholinergic toxidrome with prominent CNS effects, such as lethargy, illusions, and so-called Lilliputian hallucinations (decreasing in size over time). Onset of symptoms usually is within 30 minutes to 4 hours, and symptoms may last up to 72 to 96 hours. (Warden CR. Respiratory agents: irritant gases, riot control agents, incapacitants, and caustics. Crit Care Clin. 2005;21:719-37)

**Thursday, June 18, 2009**

**Question:**

Describe the mechanism of action of ricin.

**Answer:**

Ricin is a protein, derived from the castor bean plant, and consisting of two chains linked via two disulfide bonds. The ricin B-chain is responsible for facilitating entry into the cell via endocytosis. The ricin A-chain is then transported to the cytosol where it binds and irreversibly inactivates ribosomal 28 S rRNA. This inactivation is due to removal of an adenine residue and effectively halts protein synthesis. (Beyer NH et al. A mouse model for ricin poisoning 2009;47(3):219-25)

**Wednesday, June 17, 2009**

**Question:**

What are the major adverse effects associated with Tamiflu® (oseltamivir phosphate) when used for either treatment or post-exposure prophylaxis against the influenza virus?

**Answer:**

Headache, nausea, and vomiting. Oseltamivir is generally well-tolerated and is associated with few adverse effects when administered for either treatment or prophylaxis. Moscona A. Neuraminidase inhibitors for influenza. N Engl J Med. 2005 Sep 29;353(13):1363-73

**Tuesday, June 16, 2009**

**Question:**

In March 2009, the FDA recommended the approval of Multaq® (dronedarone) for the treatment of atrial fibrillation and atrial flutter. What well established pharmaceutical is dronedarone structurally and functionally similar to?

<p><b>Answer:</b></p> <p>Amiodarone. The omission of iodine moieties will likely make dronedarone less potentially harmful to the thyroid. Also, the addition of a methylsulfonamide group will decrease dronedarone's lipophilicity over amiodarone. Zimetbaum PJ. Dronedarone for Atrial Fibrillation ? An Odyssey. NEJM 2009 April; 360 (18): 1811-13</p>
<p><b>Monday, June 15, 2009</b></p> <p><b>Question:</b></p> <p>What is hydraulic fracturing and how does it pertain to environmental toxicology?</p> <p><b>Answer:</b></p> <p>Hydraulic fracturing is a technique used to extract oil and natural gas. In this process, fluids are injected at high pressures into the rock formations to increase the flow of oil or gas. About 40% of the injected fluids remain within the rock formation and some contend that these fluids contaminate underground sources of drinking water (USDW). In 2004, the EPA conducted a study and concluded that hydraulic fracturing posed little or no threat to USDW. <a href="http://www.epa.gov/OGWDW/uic/wells_hydrofrac.html">http://www.epa.gov/OGWDW/uic/wells_hydrofrac.html</a></p>
<p><b>Friday, June 12, 2009</b></p> <p><b>Question:</b></p> <p>Besides lowering blood glucose levels, metformin in therapeutic doses has positive effects on a number of other metabolic parameters. What are they?</p> <p><b>Answer:</b></p> <p>In persons at risk for diabetes, metformin enhances weight loss, improves lipid profiles, helps to counter insulin resistance and actually reduces the incidence of new-onset diabetes by up to 40%. The effect on long-term morbidity and mortality however has not yet been fully defined. (American Journal of Medicine. 121(2):149-157)</p>
<p><b>Thursday, June 11, 2009</b></p> <p><b>Question:</b></p> <p>A new pharmaceutical has recently been approved for, of all things, increasing eyelash length, thickness and darkness. It is indicated for individuals with hypotrichosis of the eyelashes but will certainly be used as a vanity substance by those wishing to augment their eyelashes. What are the potential adverse effects that may be associated with use of this pharmaceutical marketed under the name Latisse (bimatoprost 0.03%)?</p> <p><b>Answer:</b></p> <p>Bimatoprost 0.03% is a prostaglandin analog. It contains benzalkonium chloride as a preservative and this component may cause ocular irritation. In addition, local pruritis, conjunctival hyperemia, dry eye and redness and hyper-pigmentation of the eyelids may also occur. Interestingly, intraocular pressure may decline in some patients and this is reported to be clinically not significant. An increased pigmentation in individuals with brown iris may occur and undesired hair growth on the skin around the eyes may also occur. Finally, cystic macular edema has also been reported associated with the use of this preparation. (The Medical Letter, June 1, 2009, 51 (1313))</p>
<p><b>Wednesday, June 10, 2009</b></p> <p><b>Question:</b></p> <p>Agent Orange (2,4-D and 2,4,5-T) is the best known of the defoliants used in Vietnam and was named for the orange stripes used as identifiers on barrels used to store the compound. What other herbicide preparations were used as defoliants in Vietnam?</p> <p><b>Answer:</b></p> <p>From 1962 through 1965, small quantities of Agent Purple (also a combination of 2,4-D and 2,4,5-T), Agent Pink (2,4,5-T), Agent Green (2,4,5-T), and Agent Blue (cacodylic acid) were sprayed over forested areas in Vietnam; from 1965 through 1970, over 11 million gallons of Agent Orange (2,4,-D and 2,4,5-T) were sprayed along with lesser quantities of Agent White (2,4,5-T and picloram) and Agent Blue. From 1970 through 1971 only Agent White and Agent Blue were used for deforestation. Operation Ranch Hand was the name given to the unit responsible for conducting spraying activities from 1962 through 1971. After adjustment for confounders, a study published in 2006 showed sharpened associations between biomarkers for the dioxin TCDD and diabetes in Ranch Hand veterans and an increased all-site SEER cancer risk in the highest exposure category for TCDD. (Journal of Occupational &amp; Environmental Medicine, 2008 Mar, 50(3):330-40)</p>
<p><b>Tuesday, June 9, 2009</b></p> <p><b>Question:</b></p> <p>What is ?baboon syndrome??</p> <p><b>Answer:</b></p> <p>Baboon syndrome, first described in 2004, is a diffuse, symmetrical, erythematous eruption of the flexural areas with a V-shaped pattern on the medial thighs and diffuse erythema of the buttocks. It is seen within a few days of exposure to mercury and is unaccompanied by systemic signs or symptoms. (Current Opinion in Pediatrics, 2006 Aug, 18(4):410-6)</p>
<p><b>Monday, June 8, 2009</b></p> <p><b>Question:</b></p> <p>What are the major agents that can cause effects involving the skin in children, and what skin effects do they produce?</p> <p><b>Answer:</b></p> <p>Mercury (acrodynia, blue discoloration of the gums, acute generalized exanthematous pustulosis, and ?baboon syndrome?), arsenic (with chronic exposure, facial edema, a mildly pruritic maculopapular eruption, acral hyperkeratosis with lamellar peeling, cutaneous melanosis, and Mee's lines), dioxin-contaminated hydrocarbons (chloracne), and hypervitaminosis A (carotenoderma), (Current Opinion in Pediatrics, 2006 Aug, 18(4):410-6)</p>
<p><b>Friday, June 5, 2009</b></p> <p><b>Question:</b></p> <p>What is Laetrile and how does it cause toxicity?</p> <p><b>Answer:</b></p> <p>Laetrile is the name given to a purportedly effective chemotherapeutic agent that is particularly popular in Mexico. The drug was originally marketed for intravenous use because of its lower toxicity by this route, but it is often taken orally. The actual content varies in different preparations but can include amygdalin, isoamygdalin, or mandelonitrile glucuronide. All are cyanogenic glycosides capable of releasing cyanide and causing significant cyanide toxicity after biotransformation in the gut after ingestion. No randomized control studies have demonstrated the efficacy of Laetrile against cancer. (Cochrane Database of Systematic Reviews, 2006, (2):CD005476)</p>
<p><b>Thursday, June 4, 2009</b></p> <p><b>Question:</b></p> <p>How useful is blood-gas analysis in the evaluation of patients in whom methylene blue is used to treat methemoglobinemia?</p> <p><b>Answer:</b></p> <p>Most commercial blood-gas analyzers will report falsely low oxygen content in patients treated with methylene blue, and in at least one case this problem has led to unnecessarily prolonged intubation. Oxygen saturation measured by co-oximetry is more reliable, and clinical status is the most important indicator of the oxygenation ability. (Clinical Toxicology, 2009 Feb, 47(2):137-141)</p>
<p><b>Wednesday, June 3, 2009</b></p> <p><b>Question:</b></p> <p>What is ATRA syndrome?</p> <p><b>Answer:</b></p> <p>ATRA, or all-trans retinoic acid, is a chemotherapeutic agent that can induce remission in most cases of acute promyelocytic anemia (APL). ATRA syndrome is a potentially fatal syndrome characterized by unexplained fever, respiratory distress (including respiratory failure), and interstitial pulmonary infiltrates. Associated features in some patients include pleural and pericardial effusions, weight gain, episodic hypotension, and acute renal failure. ATRA syndrome is managed by supportive treatment, discontinuation of ATRA, and the administration of corticosteroids. (Southern Medical Journal, 2007 Sep, 100(9):899-902)</p>
<p><b>Tuesday, June 2, 2009</b></p> <p><b>Question:</b></p> <p>Temperatures in a room fire can easily reach 1000-2100° F (537-1160° C). If cyanide is flammable, how can it be a problem in fires?</p>

**Answer:**

Cyanide has a flash point of 0° F and will ignite even without a flame source at 1000° F. A prospective analysis of the toxicants generated in a test burn duplicating the circumstances of the 1981 fire at the Stardust Nightclub in Dublin, Ireland showed initial cyanide concentrations of 250 ppm, although this did not exceed the short-term lethal concentration (350 ppm) for cyanide. The concentration decreased to 10 ppm eight minutes after ignition (presumably from combustion of cyanide) and remained low thereafter. Cyanide, even if rapidly consumed in a fire, can nevertheless presumably be toxic from inhalation during the very early stages of a fire. (Journal of Burn Care & Research, 2009 Jan-Feb, 30(1):148-52)

**Monday, June 1, 2009****Question:**

What is selenite broth, and what toxic effects can be expected from its ingestion?

**Answer:**

Selenite broth, an enrichment medium used in the isolation of Salmonella species, contains 4 mg/L of sodium selenite (NaHSeO<sub>3</sub>) as well as peptone, lactose, dihydrogen sodium phosphate, and sodium dihydrogen phosphate and has a pH of 7.1. To minimize teratogenic effects to preparers, the sodium selenite is added separately to the medium. A 23-year female who ingested approximately 100 mL of selenite broth developed severe corrosive gastritis and acute tubular necrosis chiefly affecting the proximal tubules. (Saudi Journal of Kidney Diseases & Transplantation, 2009 Jan, 20(1):106-11)

**Friday, May 29, 2009****Question:**

Is there any association of recent hypermetabolic conditions with elevations of lead levels in individuals with extraarticular retained missiles (EARMs) from bullets or shrapnel?

**Answer:**

A study published in 2005 demonstrated a statistically significant rise in blood lead levels in subjects who had had a fracture within the previous 30 days but found no such increase in subjects who reported surgery, diabetes, infection, hyperthyroidism, pregnancy, or use of drugs or alcohol during the 30-day time frame. (Journal of Trauma-Injury Infection & Critical Care, 2005 Feb, 58(2):289-99)

**Thursday, May 28, 2009****Question:**

There is often a synergistic effect between the toxicological effects of drugs and other medical or surgical conditions, such as co-existing diseases, trauma, psychopathology, and exposure to other noxious agents (e.g., smoking and occupational or environmental exposures). Are medical outcomes of trauma patients who have been using cocaine different from trauma patients who have not been using cocaine?

**Answer:**

A recently published study that matched 985 trauma patients using cocaine with 4,845 trauma patients who tested negative for cocaine found no statistically significant difference in mortality or in the total incidence of complications between the two groups, although the incidence of pneumonia was higher in the cocaine-positive trauma patients. (Journal of Trauma-Injury Infection & Critical Care, 2009 Feb, 66(2):491-4)

**Wednesday, May 20, 2009****Question:**

In Europe and North America, aconite poisoning usually is associated with ingestion of the plant Aconitum napellus (monkshood, wolfsbane or devil's helmet). What is the currently recommended management for this ingestion?

**Answer:**

Management involves meticulous supportive care as there is no antidote for aconite. Atropine may be used to treat bradycardia. Otherwise standard supportive therapies including ACLS steps when necessary are indicated. In some cases involving aconite induced ventricular arrhythmias, amiodarone and/or flecainide should be considered. (Chan, TYK, 2009, Clin Tox, 47(4):279-285)

**Tuesday, May 19, 2009****Question:**

Water hemlock (Cicuta spp) is considered to be one of the most poisonous plants in North America. What part or parts of the plant are considered to be the most dangerous to ingest?

**Answer:**

All parts of the plant are poisonous but the tuberous root is known to be the most toxic part of the plant. (Schep LJ, et al, 2009, Clin Tox, 47(4):270-278)

**Monday, May 18, 2009****Question:**

Marijuana and crack cocaine are the second and third most commonly smoked substances, respectively, after tobacco. What are the short-term and long-term physiological effects of marijuana on the airways?

**Answer:**

Acutely, marijuana induces bronchodilation, not from beta-adrenergic effects but probably from direct effects of tetrahydrocannabinol on CB-1 receptors on postganglionic parasympathetic nerve endings in bronchial smooth muscle and consequent decrease in acetylcholine release. Marijuana can also promptly reverse methacholine- and exercise-induced bronchospasm in asthmatics. Some studies have noted mild chronic airflow obstruction in long-term marijuana smokers, but no decrease in diffusing capacity has ever been demonstrated. (Current Opinion in Pulmonary Medicine, 2001 Mar, 7(2):43-61)

**Friday, May 15, 2009****Question:**

Crack cocaine vaporizes at 187° C and can lead to thermal burns of the pharynx and airways. What are the most common acute pulmonary complications of inhaling crack-cocaine vapor?

**Answer:**

Cough, hemoptysis, pneumothorax, pneumomediastinum, pneumopericardium, and hemothorax are the most commonly reported complications. Most of these effects probably attributable to rises in intraalveolar pressure from the practice of inhaling deeply and then performing a Valsalva maneuver to accentuate absorption; coughing may also play a role in the barotrauma. Bullous emphysema is also seen in those who smoke cocaine chronically. (Critical Care 2008, 12(1):202)

**Thursday, May 14, 2009****Question:**

Do most users reporting ingestion of gamma-hydroxybutyrate (GHB) ingest GHB as a sole ingestant or are other substances also usually at play in these cases?

**Answer:**

GHB is usually taken with ethanol. However, although a recent study showed that 94.9% of patients presenting to the ED with GHB-like effects reported taking GHB rather than GBL, GBL was found in 37.8% of samples seized at clubs. This raises the question of whether those self-reporting ingestion of ?GHB? are unaware of GBL in the products that they are taking. (Q J Med, 2008, 101(1):23-29)

**Wednesday, May 13, 2009****Question:**

How is gamma-butyrolactone (GBL) measured in postmortem tissue, and what are precautions to be taken when interpreting these results?

**Answer:**

Solid-phase dynamic extraction (SDPE) has been used to analyze postmortem specimens for gamma-butyrolactone (GBL) and gamma-hydroxybutyrate (GHB). The results may be reported as ?GHB equivalents? (sometimes called ?total GBL?), and it is important to ask for quantitation of each compound in more than one tissue or fluid. This is because postmortem concentrations and proportions of GBL to GHB vary significantly by the kind of tissue or fluid sampled. Concentrations may also rise after death. A higher concentration of GBL than GHB in gastric contents strongly supports ingestion of GBL rather than GHB. (Therapeutic Drug Monitoring, 2008 Dec, 30(6):755-61)

**Tuesday, May 12, 2009**

**Question:**

Name a commonly available household source of gamma-butyrolactone (GBL).

**Answer:**

Although GBL is found in small quantities in some samples of unadulterated wine, it is found in higher concentrations in some superglue removers, stain removers, paint strippers, and some solvents. GBL in nail-polish remover pads has been responsible for toxicity and death in humans. (Therapeutic Drug Monitoring, 2008 Dec, 30(6):755-61)

**Monday, May 11, 2009**

**Question:**

Gamma-butyrolactone (GBL) is a precursor of gamma-hydroxybutyrate (GHB). Since possession of GBL in the United States is not currently illegal, GBL is often used in the homemade manufacture of GHB. Which is the more potent compound in terms of producing effects in the body, GBL or GHB?

**Answer:**

GBL. Equimolar amounts of GBL have been associated with a faster onset of action, higher potency, and longer duration of effects than GHB by itself even though the transport of GBL by itself across the blood-brain barrier is minimal. It may be that the danger of GHB-mediated effects from ingestion of GBL are greater than those associated with the ingestion of GHB alone. (Therapeutic Drug Monitoring, 2008 Dec, 30(6):755-61)

**Friday, May 8, 2009**

**Question:**

Urushiol is the oleoresin responsible for causing poison ivy dermatitis. How long does it take for urushiol to become fully absorbed by skin?

**Answer:**

Urushiol is easily degraded in water. However it can only be removed in clinically significant amounts if washed off immediately. At 10 minutes about 50% can be removed by washing; at 15 minutes approximately 25% can be removed; at 30 minutes only about 10% can be removed and after 30 minutes essentially all of the oil will be absorbed. (Gladman A. 2006, Wilderness & Env Med, 17(2):120-128.)

**Thursday, May 7, 2009**

**Question:**

What is the typical latency period between first exposure to arsenic (in a chronic exposure setting) and the development of the skin lesions typical of arsenic toxicity?

**Answer:**

The skin lesions (keratoses of the palms and soles) associated with chronic arsenic exposure usually appear after a usual latency period of about ten (10) years. (Smith, et al. 2000, Bull WHO, 78(9):1093-1103)

**Wednesday, May 6, 2009**

**Question:**

What is the mechanism for amiodarone induced thyrotoxicosis?

**Answer:**

Amiodarone (AM) is an iodine-rich compound that is structural similar to T3 and T4. At usual doses, amiodarone causes iodine overload up to 50-100 times the optimal daily intake. Although most patients on chronic AM treatment remain euthyroid, some may develop thyrotoxicosis (AM-induced thyrotoxicosis, AIT) or hypothyroidism. AIT is more prevalent in iodine-deficient areas and is currently subdivided in two different clinico-pathological forms (AIT I and AIT II). AIT I develops in subjects with underlying thyroid disease, and is caused by an exacerbation by iodine load of thyroid autonomous function; AIT II occurs in patients with no underlying thyroid disease and is probably consequent to a drug-induced destructive thyroiditis. Mixed or indeterminate forms of AIT encompassing several features of both AIT I and AIT II may be also observed. (Piga M, et al. 2008, Minerva Endocrinol, 33(3):213-228)

**Tuesday, May 5, 2009**

**Question:**

Excessive vomiting has been reported to be an uncommon adverse effect associated with the use of marijuana. What learned compulsive behavior reportedly characterizes this unusual clinical syndrome?

**Answer:**

Cannabinoid hyperemesis is characterized by repeated vomiting without an obvious organic cause in conjunction with learned compulsive bathing behavior using hot water. The symptoms of this syndrome usually resolve in less than 48 hours. The mechanism of cannabinoid hyperemesis is not known. (Chang YH, Windish DM. 2009, Mayo Clin Proc. 8491): 76-78

**Monday, May 4, 2009**

**Question:**

Does GHB have a licit and acceptable pharmacological use in the United States today?

**Answer:**

Yes. GHB is currently marketed in the United States under the trade name of Xyrem (sodium oxybate)(Jazz Pharmaceuticals, Palo Alto, CA) for the treatment of cataplexy in patients with narcolepsy. The prescribing of this drug is strictly limited to physicians who are registered to administer this agent. It is also marketed in some European countries as an anesthetic agent and for the treatment of alcohol withdrawal. (Abanades et al.)

**Friday, May 1, 2009**

**Question:**

Metal fume fever (MFF) is a clinical syndrome that may result from the inhalation of highly concentrated metal oxides. Which metal oxide is responsible for most cases of MFF and which other metals in oxide form have been reported to be associated with MFF?

**Answer:**

Zinc is the metal responsible for most cases of MFF. Magnesium, manganese, beryllium, copper, cadmium, nickel, aluminium, silver, antimony, tin and vanadium have also been implicated in the development of MFF cases. (Merchant J, Webby R, 2001, Emergency Medicine, 13:373-375)

**Thursday, April 30, 2009**

**Question:**

Can the serotonin syndrome result from A single therapeutic dose of an SSRI?

**Answer:**

The serotonin syndrome has been reported in a child after a single dose of fluvoxamine (Gill M, LoVecchio F, Selden B. Ann Emerg Med 1999;33:457-459)

**Wednesday, April 29, 2009**

**Question:**

Congenital cutis laxa is a condition manifested by a lack of elasticity in connective tissue resulting in sagging skin. This condition has also been reported to be associated with birth defects in infants whose mothers took which chelating agent during pregnancy?

**Answer:**

Penicillamine. The manufacturer of this drug recommends that ?penicillamine should be used in women of child bearing potential only when the expected benefits outweigh the possible hazards.?(Risher J, Amler S, 200. Neurotoxicology, 26: 691-699)

**Tuesday, April 28, 2009**

**Question:**

A number of unfortunate deaths have resulted from the ill- advised use of the chelation agent edetate disodium administered intravenously. What potentially fatal electrolyte abnormality related to chelation with this agent has been associated with these deaths?

**Answer:**

Hypocalcemia. (Baxter A, Krenzelok E. Clinical Toxicology 2008, 46:1083-1084)

**Monday, April 27, 2009****Question:**

Nitrous oxide is capable of oxidizing the cobalt atom in the vitamin B12 molecule resulting in an irreversible inhibition of methionine synthase. This mechanism may result in the development of a myeloneuropathy in individuals exposed to nitrous oxide. What profession is most commonly associated with occupational exposure to nitrous oxide and the consequent risks for myeloneuropathy?

**Answer:**

Dentists and dental professionals who administer (or abuse) nitrous oxide (Meyers L, Judge B, Clinical Toxicology 2008, 46:1095-1096)

**Friday, April 24, 2009****Question:**

What cardiac glycosides are contained in the plant *Digitalis purpurea* (Foxglove)?

**Answer:**

*Digitalis purpurea* yields digitoxin and gitoxin from its leaves and digitalin in the seeds. It does not contain digoxin, which is present only in the leaves of its cousin *Digitalis lanata*. (Ramlakhan S and Fletcher A. Eur J Emergency Medicine, 2007, 14:356-359)

**Thursday, April 23, 2009****Question:**

What is NHANES?

**Answer:**

NHANES is the "National Health and Nutrition Examination Survey" and is a program of studies designed to assess the health and nutritional status of adults and children in the United States. The survey is unique in that it combines interviews and physical examinations. NHANES is a major program of the National Center for Health Statistics (NCHS). NCHS is part of the Centers for Disease Control and Prevention (CDC) and has the responsibility for producing vital and health statistics for the Nation. Some toxicological issues including blood lead levels for various segments of the population are addressed by NHANES. ([http://www.cdc.gov/nchs/data/nhanes/nhanes\\_07\\_08/overviewbrochure\\_0708.pdf](http://www.cdc.gov/nchs/data/nhanes/nhanes_07_08/overviewbrochure_0708.pdf))

**Wednesday, April 22, 2009****Question:**

What are the MRI findings associated with "chasing the dragon" use of heroin?

**Answer:**

The most distinguishing MRI feature of chasing toxicity is the pattern of diffuse increased T2W signal within the white matter tracts of the cerebellum, brainstem and supratentorial brain including the deep grey matter structures. The key to differentiating chasing from other mimickers is the involvement of the cerebellum in a clinically nonhypertensive patient. (Bartlett E and Mikulis D. 2005, Br J Radiology, 78:997-1004)

**Tuesday, April 21, 2009****Question:**

What is the relative incorporation rate (ICR) for cocaine versus THC into human hair?

**Answer:**

THC and (especially) its main metabolite 11-nor-9-tetrahydrocannabinol-9-carboxylic acid (THC-COOH) have very low incorporation rates (ICR) into hair, with a 3600-fold difference between the ICR of cocaine and that of THC-COOH. (Muschhoff F, Madea B. 2007, Anal Bioanal Chem, 388: 1475-1494)

**Monday, April 20, 2009****Question:**

What is the standard approach to forensic drug analyses using urine and blood specimens for testing?

**Answer:**

The standard approach to forensic drug analyses for urine and blood testing is an initial immunological screening followed by a confirmation using gas chromatography/mass spectrometry (GC/MS), liquid chromatography/mass spectrometry (LC/MS), or other chromatographic procedures. (Muschhoff F, Madea B. 2007, Anal Bioanal Chem, 388: 1475-1494)

**Friday, April 17, 2009****Question:**

What is meant by the term "prescription drug diversion"?

**Answer:**

Prescription drug diversion involves the unlawful channeling of regulated pharmaceuticals from legal sources to the illicit marketplace, and can occur along all points in the drug delivery process, from the original manufacturing site to the wholesale distributor, the physician's office, the retail pharmacy, or the patient. (Inciardi JA, et al. Pain Medicine, 2007, 8(2):171-183)

**Thursday, April 16, 2009****Question:**

Aside from being bitten and seriously envenomed what is another potentially fatal occupational risk for professional (or non-professional for that matter) snake handlers?

**Answer:**

Specific IgE sensitization to snake venoms is a potentially significant and serious hazard for snake handlers who sustain repeated bites. Increasing sensitization may also take place via inhalation. This may lead to asthma symptoms and poses a potential risk for fatal anaphylaxis. Initial sensitization may occur from a bite from an unrelated species. Ongoing exposure to airborne snake venoms is a hazard for snake handlers and may be an even greater risk for known asthmatic patients who handle snakes as an avocation or vocation. (Annals of Allergy, Asthma & Immunology, 2005, 94: 600-603)

**Wednesday, April 15, 2009****Question:**

The bite of the brown recluse spider may result in a necrotizing lesion. The terms "loxoscelism", "necrotic arachnidism", or "gangrenocutaneous arachnidism" have been used to describe the clinical effects of envenomation from this spider. The clinical effects related to the bite include the necrotizing lesion and systemic effects, such as fever, chills, rash, joint pains, and hemolysis. What is the typical habitat for this spider and what are the behavioral characteristics that typify this spider?

**Answer:**

Brown recluse spiders may be found indoors or out of doors. They prefer undisturbed areas, such as boxes or furniture in garages or basements. They are nocturnal and avoid areas of human and other animal activity. These spiders generally are nonaggressive and prefer dead prey. Their bites typically are defensive and usually occur when the spider is trapped against clothing or bedding. (Furbee, et al. 2006. Clin Lab Med, 26:211- 226)

**Tuesday, April 14, 2009****Question:**

Understanding that precise numbers are nearly impossible to ascertain, approximately how many venomous snake bites are reported worldwide on an annual basis?

**Answer:**

We do not know precise figures for global snakebite epidemiology, but best estimates suggest there are more than 2.5 million venomous snakebites annually, with more than 125,000 deaths. (White J. 2000. Therapeutic Drug Monitoring, 22(1): 65-68.

**Monday, April 13, 2009**

**Question:**

What are the neurotoxic effects that have occasionally been reported in the setting of industrial exposure to cobalt?

**Answer:**

The primary neurotoxic effects reportedly associated with occupational exposure to cobalt include optic atrophy, nerve deafness and limb paresthesias. (Rizzetti MC, et al. The Lancet. 2009, 373:1144

**Friday, April 10, 2009****Question:**

Dopamine agonists used in the treatment of Parkinsons Disease have been reported to result in a variety of compulsive behaviors including pathologic gambling and hypersexuality. What other problematic compulsive behaviors have been associated with dopamine agonist therapy?

**Answer:**

Compulsive eating, excessive shopping, excessive spending, compulsive fishing, compulsive gardening and excessive engagement in hobbies have all been reported as adverse side effects of dopamine agonists. (Bostwick JM, et al. Mayo Clinic Proceedings, 2009, 84(4):310-316

**Thursday, April 9, 2009****Question:**

Ciguatera fish poisoning results from eating predatory ocean dwelling fish contaminated with ciguatoxins. Approximately how many cases of ciguatera fish poisoning are reported worldwide on an annual basis?

**Answer:**

Ciguatera fish poisoning is endemic in tropical and subtropical regions of the Pacific basin, Indian Ocean, and caribbean. Roughly 50,000 case are reported worldwide on an annual basis. MMWR, 2009, 58(11):283-285

**Wednesday, April 8, 2009****Question:**

A body stuffer typically ingests relatively small amounts of contraband drugs rapidly in order to conceal the contraband material. In this setting the contraband substances are rarely securely wrapped and thus medical effects from the contraband may be expected due to leakage of the materials and subsequent absorption into the systemic circulation. When heroin is the contraband substance being body stuffed approximately how many individuals will develop an opiate toxidrome?

**Answer:**

A recent case series reported nine percent (6/65) of patients developed signs and symptoms consistent with opiate intoxication after oral stuffing of heroin. (Jordan Mt, et al. J Emerg Med. 2009, 36(3): 250-256

**Friday, April 3, 2009****Question:**

Para-chloroaniline is found as a product in the dye, pharmaceutical and herbicide industries. What is the primary potential health threat from p-chloroaniline following unprotected exposure for workers in these settings?

**Answer:**

P-chloroaniline is a potent methemoglobin inducer. In fact, p- chloroaniline is reportedly more potent at producing methemoglobinemia than aniline itself in animal models. (Pizon AF, et al.2009. Clinical Toxicology 47(2):132-136

**Thursday, April 2, 2009****Question:**

What gas is liberated when aluminum phosphide or zinc phosphide interact with water?

**Answer:**

Phosphine gas (also known as hydrogen phosphide, phosphorus trihydride or PH3) is liberated when the above mentioned phosphides interact with moisture in the air. Phosphine gas is then the active pesticide when aluminum or zinc phosphide is used to treat grain stored in closed spaces. (Proudfoot A. 2009. Clinical Toxicology 47(2): 89-100

**Wednesday, April 1, 2009****Question:**

True or false? In contrast to poisoning with phenytoin or carbamazepine, nystagmus, dysarthria and ataxia are only rarely noted in association with valproic acid poisoning.

**Answer:**

True. The clinical findings most commonly associated with valproic acid poisoning include: CNS depression, nausea, vomiting, diarrhea, hypothermia, fever, hypotension, tachycardia, miosis, agitation, hallucinations, tremors, myoclonus, seizures and in severe cases respiratory and multi-organ failure. (Lheureux P and Hantson P. 2009. Clinical Toxicology, 47(2): 101-111)

**Tuesday, March 31, 2009****Question:**

True or False: Fluoroquinolones as a class are some of the most potent photosensitizers causing photosensitivity rashes.

**Answer:**

True. While tetracycline-class antibiotics are commonly associated with this phenomenon, they are at most weak photosensitizers, with the exception of doxycycline, which is much more potent. Other common photosensitizers include NSAIDs, tricyclic antidepressants, amiodarone, thiazide diuretics, demeclocycline, and quinidine. Morison WL. Clinical practice. Photosensitivity. New England Journal of Medicine. 350(11):1111-7, 2004 Mar 11.

**Monday, March 30, 2009****Question:**

Describe the mechanism of lead-induced anemia.

**Answer:**

Lead interferes with a variety of heme biosynthetic enzymes, including delta-aminolevulinic acid (acting to synthesize uroporphobilinogen), and ferrochelatase (used to incorporate iron into protoporphyrin). In the latter case, zinc is inserted in the place of iron, leading to an elevation of zinc protoporphyrin. Fonte R. Agosti A. Scafa F. Candura SM. Anaemia and abdominal pain due to occupational lead poisoning. Haematologica. 92(2):e13-4, 2007 Feb.

**Friday, March 27, 2009****Question:**

What illness is associated with domoic acid?

**Answer:**

Domoic acid is associated with amnesic shellfish poisoning. Symptoms include nausea/vomiting, diarrhea, abdominal cramps, headache, and short-term memory loss. More severe cases can present with severe respiratory secretions, labile blood pressure, seizures, and coma. Neuroexcitation is believed to be due to kainate receptor stimulation. Jeffery B, Barlow T, Moizer K, Paul S, Boyle C. Amnesic shellfish poison. Food Chem Toxicol. 2004 Apr;42(4):545-57.

**Thursday, March 26, 2009****Question:**

Which potent hallucinogenic drug's street name is based on its chemical structure?

**Answer:**

Bromo-drugonfly. With a little imagination, the chemical structure looks like a fly. ref: A novel (benzodifuranyl)aminoalkane with extremely potent activity at the 5-HT2A receptor' by M. A. Parker, D. Marona-Lewicka, V. L. Lucaites, D. L. Nelson, and D. E. Nichols in J. Med. Chem. 41(26): 5148-5149 (1998)



**Wednesday, March 25, 2009**

**Question:**

What is hypoglycin A?

**Answer:**

Hypoglycin A is a toxin found in the unripened Jamaican ackee fruit. It can produce vomiting, drowsiness, and hypoglycemia, and has been shown to inhibit the activity of short and medium chain acyldehydrogenases. Blake OA, Bennink MR, Jackson JC. Ackee (Blighia sapida) hypoglycin A toxicity: dose response assessment in laboratory rats. Food Chem Toxicol. 2006 Feb;44(2):207-13.

**Tuesday, March 24, 2009**

**Question:**

Which herbal medications may be associated with the development of hyperkalemia?

**Answer:**

Noni juice, alfalfa, dandelion, horsetail, nettle, milkweed, and hawthorne berries. (J Intensive Care Med, 2005 Sep 1, 20(5):272-290)

**Monday, March 23, 2009**

**Question:**

What pharmacologically based public-health measure may reduce the risk of arsenic-induced skin lesions in countries (such as Bangladesh) with high concentrations of arsenic in well water?

**Answer:**

B vitamins and antioxidants. (Environ Health Perspect, 2008 Aug, 116(8):1056-1062)

**Friday, March 20, 2009**

**Question:**

What are three antiepileptic medications that have been reported to be causally associated with metabolic acidosis?

**Answer:**

Acetazolamide, zonisamide, and topiramate (Neurology, 2004 Nov 23, 63(10 Suppl 4):S24-S29)

**Thursday, March 19, 2009**

**Question:**

What are chemical reactivity sheets?

**Answer:**

They are consolidated tables of health-and-safety information for chemical agents. Although they were designed as improvements on Material Safety Data Sheets, they may still fail to identify critical information or falsely attribute hazards to chemicals. (J Chem Health Safety, 2006 Sep-Oct, 13(5):29-34)

**Wednesday, March 18, 2009**

**Question:**

What drugs have been associated with the development of progressive multifocal leukoencephalopathy (PML)?

**Answer:**

Classic cytotoxics and immunosuppressants (e.g., cyclophosphamide, methotrexate, and mycophenolate mofetil) as well as more recently introduced drugs, such as the B-cell-depleting monoclonal anti-CD20 antibody rituximab, the T-cell-depleting monoclonal anti-CD52 antibody alemtuzumab, and the T-cell-inactivating monoclonal anti- $\alpha_2$  integrin lymphocyte function-associated antigen-1 antibody efalizumab. (The Lancet Neurology, 2009 Jan, 8(1):28-31)

**Tuesday, March 17, 2009**

**Question:**

True or False: In building fires, the vertical and horizontal dispersion of toxic gases has been found to be relatively uniform.

**Answer:**

False. Concentrations of toxic gasses in fires are indeed relatively constant at a given height over surprisingly long distances from the origin of the fire but are significantly lower in the lower half of a given vertical cross-section of a burning corridor. The time needed to achieve maximal concentrations is also lower in the upper zone of heated air. (J Fire Sciences, 2008 Jan, 268(1):45 [18 pages])

**Monday, March 16, 2009**

**Question:**

What is the comet assay?

**Answer:**

Also known as single-cell gel electrophoresis (SCGE), the comet assay, so named because of the comet-like appearance of intact (the head of the comet) and damaged (the tail of the comet) DNA, is a simple, rapid, and sensitive tool for assessing DNA damage in eukaryotic and some prokaryotic cells. (Cell Biol and Toxicol, 2009 Feb, 25(1))

**Friday, March 13, 2009**

**Question:**

True or False: The only currently used mouthwash ingredient to which death has been attributed is ethanol.

**Answer:**

False. A death from ingestion of three liters of an essential-oil-containing mouthwash was attributed to the terpenes that were the active ingredients in the mouthwash. (J Intensive Care Med, 2003 May-Jun, 18(3):150-155)

**Thursday, March 12, 2009**

**Question:**

What are the three leading mechanistic hypotheses proposed for the immunological basis of idiosyncratic drug reactions?

**Answer:**

The hapten hypothesis, the danger hypothesis, and the PI (pharmacological-interaction) hypothesis. (Annu Rev Pharmacol Toxicol 2007; 47:513-539)

**Wednesday, March 11, 2009**

**Question:**

Synthetic zeolites are rapidly replacing phosphates as builders in laundry detergents. What toxic effects can zeolites in these detergents have?

**Answer:**

Local irritation but not systemic toxicology may be expected. (Arch Toxicol, 2009 Jan, 83(1))

**Tuesday, March 10, 2009**

**Question:**

True or False: Firefighters are often exposed to hazardous substances (including carbon monoxide, hydrogen cyanide, hydrogen chloride, benzene, and sulfur dioxide), but their serum biochemical profiles are not significantly different from controls.



**Answer:**

False. A recent study in Saudi Arabian firefighters showed statistically significant differences in liver function, kidney function, serum lipid profile, cortisol, creatine kinase, lactate dehydrogenase, and iron between firefighters and controls. (J Occ Med Toxicol, 2008 Dec 11, 3:33)

**Monday, March 9, 2009****Question:**

What are the laboratory indicators of arsenic-induced nephrotoxicity?

**Answer:**

Urinary blood, and increased urinary protein, ketones, and bilirubin (Internet J Toxicol, 2008 5(2))

**Friday, March 6, 2009****Question:**

True or False: All of the fatalities from the 1995 sarin attack on the Tokyo subway system resulted from exposure to liquid sarin rather than sarin vapor and occurred within 48 hours of the exposure.

**Answer:**

False. One 51-year-old man who inhaled sarin went into cardiac arrest and was successfully resuscitated but did not regain consciousness. He died 15 months later, and autopsy findings including findings consistent with dying-back peripheral neuropathy. This is the only such case of this kind of neuropathy reported after exposure to a nerve agent. (Neurology, 1998 Oct, 51(4):1195-1197)

**Thursday, March 5, 2009****Question:**

What is Bromo-Dragonfly?

**Answer:**

Bromo-Dragonfly, also called ABDF, is a psychedelic hallucinogen recently banned in Denmark after the overdose death of an 18-year-old female. (Forensic Sci International, 2009 Jan 10, 183(1-3):91-97)

**Wednesday, March 4, 2009****Question:**

True or False: Since passage of the Dietary Health Supplement Health and Education Act of 1994, herbal-poisoning exposures reported to poison control centers have dropped by 20%.

**Answer:**

False. They have actually increased by 344%, with 24,412 exposures being reported in 2003. (J Pharmacy Pract, 2005, 18(3), 188-208)

**Tuesday, March 3, 2009****Question:**

What is the primary cytochrome P450 enzyme responsible for metabolizing nicotine?

**Answer:**

CYP2A6, and variability in the activity of this enzyme contributes to susceptibility to tobacco dependence, response to therapy, and risk for lung cancer. (Annu Rev Pharmacol Toxicol, 2009 Feb, 49:57-71)

**Monday, March 2, 2009****Question:**

What findings predominate in renal biopsies of patients with lithium toxicity?

**Answer:**

Chronic tubulointerstitial nephropathy (CTIN), cortical and medullary tubular cysts and dilatation, and focal segmental and global glomerulosclerosis (J Am Soc Nephrol, 2000, 11:1439-1448)

**Friday, February 27, 2009****Question:**

Cold allodynia (dysesthesia when touching cold water or cold objects) is characteristic of ingestion of fish containing what toxins?

**Answer:**

Ciguatoxins. Note that cold allodynia is often incorrectly termed "temperature reversal." (Lancet Neurol, 2005 Apr, 4(4):219-228)

**Thursday, February 26, 2009****Question:**

True or False: The glycol ethers, particularly ethylene glycol monomethyl ether (EGME) and ethylene glycol monoethyl ether (EGEE), have been causally linked to reproductive effects in occupationally exposed workers.

**Answer:**

False. The evidence is still inconclusive. (Toxicol Letters, 2005 Mar 28, 156(1):13-28)

**Wednesday, February 25, 2009****Question:**

From a toxicological perspective, what do pennyroyal, tansy, black cohosh root, blue cohosh root, cotton root bark, angelica root, rue, motherwort, and mandrake have in common?

**Answer:**

They have all enjoyed popularity throughout history as abortifacients (Acad Emerg Med, 2000 Jul, 7(7):824-829)

**Tuesday, February 24, 2009****Question:**

Comfrey, or "knitbone" (Symphytum officinale), has long been used in herbal medicine for a variety of ailments, especially disorders of bone and teeth. What is the predominant hepatic toxicity following comfrey ingestion, and what compounds are responsible for this toxicity?

**Answer:**

Hepatotoxic pyrrolizidine alkaloids such as lasiocarpine and symphytine can cause hepatic veno-occlusive disease (and can also be mutagenic and possibly carcinogenic), presumably by being transformed by hepatic microsomal enzymes into highly reactive pyrroles that act as alkylating agents. (Public Health Nutrition, 2000, 3:501-508 and BMC Bioinformatics 2006, 7(Suppl 2):S16)

**Monday, February 23, 2009****Question:**

Drug associated movement disorders place elderly patients at risk for what problem?

**Answer:**

Hip fracture due to falls. (Freedman, R. NEJM, 2003; 349:1738-1749)

**Friday, February 20, 2009**

**Question:**

Adverse drug related events (ADRE?s) are thought to account for approximately what percentage of ED visits per annum in the United States?

**Answer:**

ADRE?s are thought to account for as many as 28% of ED visits in the US and as many as 30% of hospital admissions. (Hohl, CM, et al. Academic Emergency Medicine, 2005, 12:197-205)

**Thursday, February 19, 2009****Question:**

What is the specific risk to the fetus associated with maternal use of benzodiazepines during the first trimester of pregnancy? How about during the late third trimester?

**Answer:**

Benzodiazepines should not be used in the first trimester because of the risk of oral clefts. Use of benzodiazepines late in the third trimester may cause the floppy infant syndrome or neonatal withdrawal. (Fricchione G. NEJM, 2004, 351: 675-682)

**Wednesday, February 18, 2009****Question:**

Buspirone is a nonbenzodiazepine anxiolytic with efficacy in the treatment of generalized anxiety disorder. Can this agent be used as single therapy for the treatment of depression as well?

**Answer:**

No. Buspirone has no antidepressant effect and should not be used alone to treat anxiety that co-exists with depression.

(Fricchione G. NEJM, 2004, 351: 675-682)

**Tuesday, February 17, 2009****Question:**

What is plumbism?

**Answer:**

Plumbism is clinical lead poisoning. Farrell SE, et al. 1999 Acad Emerg Med 6(3):208-212

**Friday, February 13, 2009****Question:**

Which statin drug is the most common cause for statin induced myopathy and why.

**Answer:**

Simvastatin is probably responsible for more cases of myopathy simply by virtue of the fact that it is currently the best selling and most widely prescribed statin drug. The Medical Letter, October 20,2008, issue 1297.

**Thursday, February 12, 2009****Question:**

The compound melamine has recently been in the news relative to its presence in infant formula and milk products causing illness (and deaths) among infants in China. Why was melamine put into these products?

**Answer:**

Melamine, a nitrogen containing compound) was illegally added to products such as milk and gluten to falsely boost the apparent protein content; commonly used lab assays for protein content in food do not distinguish between amino acid nitrogen and non-protein nitrogen. The Medical Letter, October 20,2008, issue 1297.

**Wednesday, February 11, 2009****Question:**

What is ?Crystal Dex??

**Answer:**

?Crystal Dex? is the crystalline product resulting from the single phase acid base extraction technique sued by some abusers seeing to obtain a purified form of dextromethorphan. Hendrickson RG and Cloutier R, 2007, J Emerg Med 32(4):393-396.

**Tuesday, February 10, 2009****Question:**

The following terms are synonyms for what drug often used for its recreational and stimulant properties: Qat, Gat, Muhulo, Musitate, Tschat and Miraa?

**Answer:**

These are synonyms for Khat (Catha edulis). Cathinone is the main stimulant found in Khat leaves. Bentur Y, et al. 2008, Clin Tox, 46:206-210.

**Monday, February 9, 2009****Question:**

True or false: Wikipedia is a reliable source for online drug information

**Answer:**

False. A recent study concluded Wikipedia has a more narrow scope, is less complete, and has more errors of omission than a comparator database. They further noted that Wikipedia may be a useful point of engagement for consumers, but is not authoritative and should only be a supplemental source of drug information. Clausen KA et al. 2008. Annals of Pharmacotherapy, 42(12): 1814-1921

**Friday, February 6, 2009****Question:**

What are the constituents of Intralipid 20%?

**Answer:**

Intralipid 20% is composed of 20% soybean oil, 1.2% egg yolk phospholipids, 2.25 % glycerin and water. Corman SL, 2007, Anns Pharmacotherapy, 41:1873-1877.

**Thursday, February 5, 2009****Question:**

What is the difference in risk for sudden cardiac death in users of typical antipsychotic drugs versus the risk for sudden death in users of atypical antipsychotic drugs?

**Answer:**

Current users of typical and of atypical antipsychotic drugs have similar, dose related increased risk for sudden cardiac death. Ray WA, et al. NEJM 2009; 360:225-235.

**Wednesday, February 4, 2009****Question:**

What are the reported risks for infants born to mothers who took an SSRI during the third trimester?

**Answer:**

Higher risk of requiring treatment in an ICU possibly related to a withdrawal reaction and of developing persistent pulmonary hypertension. The Medical Letter, 50(1299), November 17, 2008

**Tuesday, February 3, 2009****Question:**

What is the fractional conversion of cocaine to cocaethylene in the presence of substantial blood ethanol concentrations?

**Answer:**

Approximately 17 % if cocaine is converted to cocaethylene in the presence of substantial blood ethanol concentrations. Harris DS, et al. 2003. Drug and Alcohol Dependence 72:169-182

**Monday, February 2, 2009****Question:**

What does the 'n' in n-hexane stand for?

**Answer:**

The 'n' stands for 'normal' to distinguish it from the isoforms of hexane, 3-methyl pentane, 2-methyl pentane and 2,3 methyl butane. Dick FD. Solvent neurotoxicity, 2006, Occ Env Med, 63:221-226

**Friday, January 23, 2009****Question:**

Describe the clinical effects of capsaicin.

**Answer:**

Capsaicin, derived from Capsicum annuum, is a potentially neurotoxic substance capable of causing burns on exposed skin and mucous membranes. Inhalation of high doses of capsaicin may cause coughing and bronchospasm as well as gastro-intestinal injury. It has also been reported to result in death. Snyman T. Stewart MJ. Steenkamp V. A fatal case of pepper poisoning. Forensic Science International. 124(1):43-6, 2001 Dec 15.

**Thursday, January 22, 2009****Question:**

Describe the mechanism of action of sitagliptin for use in type II diabetes mellitus.

**Answer:**

Sitagliptin is a dipeptidyl peptidase 4 (DPP-4) inhibitor. By inhibition of DPP-4, sitagliptin enhances post-prandial levels of active glucagon-like peptide-1 (GLP-1), subsequently leading to a rise in insulin release and a decrease in glucagon. Zerilli T. Pyon EY. Sitagliptin phosphate: a DPP-4 inhibitor for the treatment of type 2 diabetes mellitus. Clinical Therapeutics. 29(12):2614-34, 2007 Dec.

**Wednesday, January 21, 2009****Question:**

True or False: Patients with hyperthyroidism are more prone to develop digoxin toxicity.

**Answer:**

False. Patients with HYPOTHYROIDISM are reportedly more susceptible to the effects of digoxin. El-Salawy SM. Lowenthal DT. Ippagunta S. Bhinder F. Clinical Pharmacology and Physiology Conference: digoxin toxicity in the elderly. International Urology & Nephrology. 37(3):665-8, 2005.

**Tuesday, January 20, 2009****Question:**

Which chemical is produced as a metabolite of both chloral hydrate and trichloroethylene?

**Answer:**

Both of these chemicals are metabolized to trichloroethanol. This may result in inaccurately attributing trichloroethylene overdose to chloral hydrate. Trichloroethylene, while commonly used as a degreasing solution, can also be found as a solvent in certain commercial glues, and has been reported to be abused. Jones GR. Singer PP. An unusual trichloroethanol fatality attributed to sniffing trichloroethylene. Journal of Analytical Toxicology. 32(2):183-6, 2008 Mar.

**Monday, January 19, 2009****Question:**

What is the estimated incidence of acute dystonias associated with metoclopramide?

**Answer:**

The incidence of acute dystonias due to metoclopramide is estimated to be 0.2% (1 in 500). However, this rate may be higher due to suspected under-reporting. Bateman DN. Rawlins MD. Simpson JM. Extrapyramidal reactions with metoclopramide. British Medical Journal Clinical Research Ed.. 291(6500):930-2, 1985 Oct 5.

**Friday, January 16, 2009****Question:**

Describe the physiologic mechanism theorized to be at play in drug-associated extrapyramidal reactions.

**Answer:**

The extrapyramidal system modulates motor function via excitatory cholinergic and inhibitory dopaminergic neurotransmission. Certain medications, including neuroleptics and some antiemetics, cause dopaminergic blockade, thus interfering with proper modulation of this motor system, leading to extrapyramidal motor effects. Dingli K. Morgan R. Leen C. Acute dystonic reaction caused by metoclopramide, versus tetanus. BMJ. 334(7599):899-900, 2007 Apr 28.

**Thursday, January 15, 2009****Question:**

Describe the potential long-term effects related to significant carbon monoxide exposure.

**Answer:**

Patients with significant exposure to carbon monoxide may be at risk for delayed neurologic sequelae including cognitive impairment, dementia, amnesia, psychosis, paralysis, cortical blindness, and peripheral neuropathy, Parkinsonism, and chorea. In addition, a recent prospective cohort study also reported an association between carbon monoxide exposure and increased mortality in patients with myocardial injury (troponin I =0.7 ng/ml or CK-MB =5.0 ng/ml) at the time of exposure. Henry CR. Satran D. Lindgren B. Adkinson C. Nicholson CI. Henry TD. Myocardial injury and long-term mortality following moderate to severe carbon monoxide poisoning. JAMA. 295(4):398-402, 2006 Jan 25.

**Wednesday, January 14, 2009****Question:**

True or False: All medications causing QT interval prolongation place patients at higher risk for torsades de pointes?

**Answer:**

False. While this statement is true in most instances, some medications may increase the QT interval but are not generally associated with torsades. Examples of these include amiodarone, quinidine, and tricyclics. Medications that prolong the QT interval are not always associated with torsades, and conversely, medications associated with torsades do not always increase the QT interval. Kao LW. Furbee RB. Drug-induced q-T prolongation. Medical Clinics of North America. 89(6):1125-44, x, 2005 Nov

**Tuesday, January 13, 2009****Question:**

Describe what is referred to by each color in the 4 color-coded diamond National Fire Protection Association (NFPA) 704 system placard for hazardous materials information.

**Answer:**

Red refers to flammability, blue refers to health hazard, yellow refers to chemical reactivity, and white refers to other miscellaneous information, such as radioactivity, biological hazards, oxidizing agents, corrosives, etc. National Fire Protection Association (NFPA) Technical Committee on Hazardous Materials Response Personnel: NFPA 704: Standard System for the Identification of the Hazards of Materials for Emergency Response, Quincy, MA, NFPA, 2007

**Monday, January 12, 2009**

**Question:**

What is polymer fume fever?

**Answer:**

Polymer fume fever is a self-limited systemic illness that primarily presents with pulmonary symptoms. Polymer fume fever is caused by inhalation of heated polytetrafluoroethylene (Teflon) above 350-400 degrees C. Shusterman DJ. Polymer fume fever and other fluorocarbon pyrolysis-related syndromes. Occupational Medicine. 8(3):519-31, 1993 Jul-Sep.

**Friday, January 9, 2009**

**Question:**

Which of the following would be an atypical presenting sign or symptom of Q fever?

- A: Fever
- B: Myalgias
- C: Hepatitis
- D: Cholecystitis
- E: Pneumonia

**Answer:**

d. The classic presentation is a flu-like illness with fevers, sweats, cough, myalgias, and arthralgias. Acute acalculous cholecystitis has been described with Q fever but it has only been described rarely (although 2 recent cases in US military personnel returning from Iraq have been reported). (Hartzell JD et al. Q fever: Epidemiology, diagnosis and treatment. 2008. Mayo Clin Proceedings, 83(5): 574-579)

**Thursday, January 8, 2009**

**Question:**

True or false:the use of alcohol containing mouthwash is associated with the development of oropharngeal cancer?

**Answer:**

False. While some have posited a causal association between the use of alcohol containing mouthwash and the development of oropharyngeal cancer over the past 25 years there have been nine epidemiological studies reported on this topic. The weight of the evidence from these studies strongly suggests that the use of alcohol containing mouthwash does not increase the risk for oropharngeal cancer. (Cole et al. Alcohol containing mouthwash and oropharyngeal cancer. 2003. Journal of the American Dental Association, 134:1079-1083.

**Wednesday, January 7, 2009**

**Question:**

Name four common household (non-beverage) products that may contain ethanol

**Answer:**

Some mouthwash products may contain 15-27% ethanol; Some aftershave products may contain 50-90% ethanol; Some hairspray products may contain 25-80% ethanol; some cough and cold preparations may contain up to 25% ethanol (Khan F et al. 1999, Overlooked sources of ethanol. 17(6):985-988

**Tuesday, January 6, 2009**

**Question:**

A recent epidemic of melamine poisoning arose from tainted infant formula in China. This epidemic affected nearly 300,00 children in China with more than 50,000 hospitalized and a number of deaths.

What was the basis of the pathology involved in these melamine affected children?

**Answer:**

Melamine, at high doses, may induce the formation of genitourinary stones with subsequent development of renal failure. Melamine stones are not completely radiopaque and are usually formed by melaine and its metabolite cyanuric acid combined with uric acid or in a protein matrix with uric acid, protein, and phosphate. (Ingelfinger JR. Melamine and the global implications of food contamination. 2008. NEJM, 359(26):2745-2748.

**Monday, January 5, 2009**

**Question:**

Q fever is a zoonotic infection caused by Coxiella burnetti.

Over 30 cases have been reported among US military personnel deployed to Iraq and Afghanistan over the past few years and this disease is of concern as a potential terrorist weapon. Of special concern is the fact that C. burnetti is highly infectious with a single or just a few organisms necessary for disease induction. How are humans usually exposed to Q fever?

**Answer:**

Humans are exposed to C. burnetti when animals shed the organism into feces, urine, milk or products of conception. (Hartzell JD et al. Q fever: Epidemiology, diagnosis and treatment. 2008. Mayo Clin Proceedings, 83(5): 574-579)

**Wednesday, December 24, 2008**

**Question:**

In one series of tricyclic antidepressant overdoses, all patients had sinus tachycardia, a corrected QT interval of > 418 ms, and a terminal QRS vector between 130 and 270 degrees. How common is this constellation of findings in cardiograms performed in the Emergency Department?

**Answer:**

Using the above criteria, a computer aided search of >15,000 ECGs found the likelihood of meeting all criteria to be 1%. The positive and negative predictive values of the above criteria were subsequently found to be 66% and 100% in a population of 299 overdose patients. Niemann, J. T., H. A. Bessen, et al. (1986). Electrocardiographic criteria for tricyclic antidepressant cardiotoxicity. Am J Cardiol 57(13): 1154-9.

**Tuesday, December 23, 2008**

**Question:**

True or false, pediatric ingestions of clonidine commonly results in delayed (>6 hours) toxicity?

**Answer:**

False. In one series of clonidine ingestions in 113 children under twelve, onset of full clinical effects was complete within 4 hours in all cases. In addition, in the 61 children who ingested less than 0.3 mg, none had coma, respiratory depression or hypotension. Spiller, H. A., W. Klein-Schwartz, et al. (2005). Toxic clonidine ingestion in children. J Pediatr 146(2): 263-6.

**Monday, December 22, 2008**

**Question:**

What characteristics differentiate rodenticide superwarfarins from warfarin?

**Answer:**

(1) Greater affinity for vitamin K-12-3-epoxide reductase; (2) the ability to disrupt the vitamin K1-epoxide cycle at more than one point; (3) hepatic accumulation; and (4) unusually long biological half-lives due to high lipid solubility and enterohepatic circulation have been credited for the greater potency and duration of action of the long-acting anticoagulant rodenticides. Watt, B. E., A. T. Proudfoot, et al. (2005). Anticoagulant rodenticides. Toxicol Rev 24(4): 259-69.

**Friday, December 19, 2008**

**Question:**

What laboratory finding is suggestive for the diagnosis of bromism?

**Answer:**

Negative anion gap with hyperchloremia. Bromides produce a falsely elevated chloride level, which leads to a negative anion gap calculation. A chloride level greater than 115 meq/L is suggestive of bromide ingestion. (Horowitz BZ. Bromism from excessive cola consumption. Journal of Toxicology: Clinical Toxicology. 1997;35(3):315-20.

**Thursday, December 18, 2008**

**Question:**

What is the major risk factor for the development of allopurinol hypersensitivity syndrome?

**Answer:**

Renal insufficiency. Allopurinol hypersensitivity syndrome (AHS) is a potentially life-threatening cutaneous adverse reaction. It has been hypothesized that the accumulation of allopurinol, or its metabolites, in patients with renal insufficiency is the major cause for allopurinol hypersensitivity syndrome. (Lee HY, Ariyasighe JT, Thirumoorthy T. Allopurinol hypersensitivity syndrome: a preventable severe cutaneous adverse reaction? Singapore Med J. 2008 May;49(5):384-7.)

**Wednesday, December 17, 2008**

**Question:**

What mineral, other than amphibole asbestos, has been causally linked to mesothelioma?

**Answer:**

Erionite. Erionite is a fibrous mineral found in zeolite stones used to build houses in the Cappadocia region of Turkey. (Baris YI, Sahin AA, Ozesmi M, et al. An outbreak of pleural mesothelioma and chronic fibrosing pleurisy in the village of Karain/Urgup in Anatolia. Thorax 1978; 33:181?192.)

**Tuesday, December 16, 2008**

**Question:**

What electrocardiogram abnormality has been associated with arsenic trioxide (Trisenox) use?

**Answer:**

QTc prolongation. Arsenic trioxide causes QTc prolongation by blocking the delayed rectifier K+ current. (Drolet B, Simard C, Roden DM. Unusual effects of a QT-prolonging drug, arsenic trioxide, on cardiac potassium currents. Circulation. 2004 Jan 6;109(1):26-9.)

**Monday, December 15, 2008**

**Question:**

What condition is associated with ?chasing the dragon??

**Answer:**

Toxic spongiform leukoencephalopathy (TSL). ?Chasing the dragon,? or ?chinesing? is a method of inhaling opium or heroin. Users heat the powdered drug on aluminium foil and inhale the smoke. TSL is a disease of the white matter that causes vacuolization of the oligodendroglia. The clinical features of TSL include memory loss, dementia, coma, and death. (Hill MD, Cooper PW, Perry JR. Chasing the dragon - neurological toxicity associated with inhalation of heroin vapour: case report CMAJ. 2000 Jan;162(2):236-8)

**Friday, December 12, 2008**

**Question:**

What effect is associated with Coprinus atramentarius ingestion?

**Answer:**

Disulfiram effect. The Coprinus atramentarius mushroom contains the toxin coprine. Coprine and its major metabolite both inhibit aldehyde dehydrogenase. If the Coprinus atramentarius mushroom is ingested with ethanol, the accumulation of acetaldehyde will cause flushing, nausea, and vomiting. (Carlsson A, et al. On the disulfiram-like effect of coprine, the pharmacologically active principle of Coprinus atramentarius. Acta Pharmacol Toxicol (Copenh). 1978 Apr;42(4):292-7)

**Thursday, December 11, 2008**

**Question:**

What abnormalities have been associated with the use of fenfluramine-phentermine?

**Answer:**

Valvular heart disease. In 1997, researchers at the Mayo Clinic presented a report on 24 patients who developed valvular insufficiency while taking the combination diet pill Fen-phen. The mitral valve was the most commonly affected valve, followed by the aortic valve. Patients with left sided valve dysfunction developed pulmonary hypertension. (Graham DJ, Green L. Further cases of valvular heart disease associated with fenfluramine-phentermine. N Engl J Med. 1997; 337: 635?8)

**Wednesday, December 10, 2008**

**Question:**

Which cancer has been associated with the use of diethylstilbestrol?

**Answer:**

Diethylstilbestrol (DES) is a transplacental carcinogen. Maternal use of this synthetic estrogen has been associated with vaginal cancer (clear cell adenocarcinoma) in female offspring. Approximately 0.1% of DES exposed offspring develop vaginal cancer, typically after the onset of puberty. DES exposure is also associated with reproductive tract structural abnormalities, pregnancy complications, and infertility in female offspring. Noncancerous epididymal cysts have been observed in male offspring. (Newbold RR. Prenatal exposure to diethylstilbestrol (DES). Fertility and Sterility. 2008 Feb;89(2 Suppl):e55-6.)

**Monday, December 8, 2008**

**Question:**

True or false: There are currently a wide variety of oximes available to practitioners for use in the United States in the treatment of organophosphate related toxicity.

**Answer:**

False. While a number of different oxime compounds are indeed available in various different countries around the world. The only oxime available for use in the United States currently is pralidoxime chloride. (Roberts DM and Aaron CK. Management of acute organophosphate pesticide poisoning. 2007, Br Med J. 334:629-634

**Friday, December 5, 2008**

**Question:**

Abuse of 1-benzylpiperazine (BZP), 1-(3-trifluoromethylphenyl)piperazine (3-TFMPP), and 1-(3-chlorophenyl)piperazine (3-CP) is becoming increasingly popular in what setting?

**Answer:**

These compounds have become popular as dugs of abuse at a variety of dance clubs where they may be marketed as legal alternatives to MDMA.zzz(Elliot S, Smith C. Investigation of the first deaths in the United Kingdom involving the detection and quantitation of the piperazines BZP and 3-TFMPP. J Anal Toxicol. 2008 Mar;32(2):172-7.)

**Thursday, December 4, 2008**

**Question:**

Abuse of what substance can lead to positive trichloroethanol in the absence of exposure to chloral hydrate?

**Answer:**

Sniffing or inhaling contact cement. Some contact cement products may contain trichloroethylene which is metabolized to trichloroethanol and may cause positive trichloroethanol levels at autopsy. (Jones GR, Singer PP. An unusual trichloroethanol fatality attributed to sniffing trichloroethylene. J Anal Toxicol. 2008 Mar;32(2):183-6)

**Wednesday, December 3, 2008****Question:**

Finding trichloroethanol on autopsy toxicology tests suggests abuse of what drug?

**Answer:**

Chloral hydrate is metabolized to trichloroethanol and commonly causes positive trichloroethanol levels at autopsy. (Jones GR, Singer PP. An unusual trichloroethanol fatality attributed to sniffing trichloroethylene. J Anal Toxicol. 2008 Mar;32(2):183-6.)

**Tuesday, December 2, 2008****Question:**

What problem with measuring 1,3-propanediol by GC-MS requires clinicians to maintain a high level of suspicion for this toxicant?

**Answer:**

1,3-propanediol is used as the internal standard used in GC-MS for measuring glycols. So, a person poisoned by 1,3-propanediol won't have a corresponding peak by GC-MS because it will be hidden with in the internal standard peak. The internal standard peak may seem unusually large which should prompt repeat GC-MS using a different standard. (Garg U, Frazee CC 3rd, Kiscoan M, Scott D, Peterson B, Cathcart D. A fatality involving 1,3-propanediol and its implications in measurement of other glycols. J Anal Toxicol. 2008 May;32(4):324-6)

**Monday, December 1, 2008****Question:**

What compounds are used instead of ethylene glycol in "non-toxic" anti-freeze? Are they potentially harmful?

**Answer:**

Antifreeze traditionally contains ethylene glycol, but some brands marketed as low toxicity or "non-toxic" use 1,2-propanediol (aka propylene glycol) or 1,3-propanediol (aka trimethylene glycol or 1,3-dihydroxypropane). Although less toxic than ethylene glycol, both compounds have been implicated as a cause of death with blood levels in the 400 mg/dL range. (Garg U, Frazee CC 3rd, Kiscoan M, Scott D, Peterson B, Cathcart D. A fatality involving 1,3-propanediol and its implications in measurement of other glycols. J Anal Toxicol. 2008 May;32(4):324-6)

**Wednesday, November 26, 2008****Question:**

Which of the following findings suggests heroin use rather than codeine use?

- a. Serum morphine:serum codeine < 1
- b. Serum morphine:serum codeine > 1
- c. Urine morphine:urine codeine < 1
- d. Urine morphine:urine codeine > 1
- e. Negative 6'-acetylmorphine (6-AM) in the urine

**Answer:**

B. Serum morphine to serum codeine ratio above unity (ie greater than 1) suggests heroin use. Positive 6-AM indicates heroin use, though it has low sensitivity as it is present for only a short time frame and thus difficult to detect. (Ceder G, Jones AW. Concentration ratios of morphine to codeine in blood of impaired drivers as evidence of heroin use and not medication with codeine. Clin Chem. 2001 Nov;47(11):1980-4)

**Tuesday, November 25, 2008****Question:**

What beta-2 agonist used in veterinary medicine has recently been reported as an adulterant in heroin?

**Answer:**

Clenbuterol is a beta-2 adrenergic agonist used in veterinary medicine as a bronchodilator. It is not approved for use in humans. It has reportedly been used illicitly as a doping agent by some professional and amateur athletes. Reports of heroin adulterated with clenbuterol resulting in adverse reactions have been reported in several states including New York, New Jersey, North Carolina, South Carolina, Connecticut, and Pennsylvania. (Werder G, Arora G, Frisch A, Aslam S, Imani F, Missri J. Clenbuterol-contaminated heroin: cardiovascular and metabolic effects. A case series and review. Conn Med. 2006 Jan;70(1):5-11)

**Monday, November 24, 2008****Question:**

What material is toxicologically unique in that it has the potential to act as both a chemical and a radiological toxicant?

**Answer:**

Depleted uranium (DU). DU has the capacity to cause renal injury as a chemical toxicant. Radiologically, DU emits alpha, beta and gamma radiation with alpha emission being the primary hazard if inhaled, ingested or if present in open wounds. (Sztajnkrzyer MD, Otten EJ. 2004. Chemical and radiological toxicity of depleted uranium. Military Medicine, 169(3):212-216)

**Friday, November 21, 2008****Question:**

In the early 1980's a number of young adults in northern California developed a dense parkinsonian syndrome following the IV use of what was thought by them to be synthetic heroin. Subsequent investigation determined this material to contain what chemical that has also been used to develop an animal model for Parkinson's Disease?

**Answer:**

1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). (Fukuda T.

Neurotoxicity of MPTP. 2001. Neuropathology, 21:323-332)

**Thursday, November 20, 2008****Question:**

Acute poisoning involving nutmeg primarily involves nausea, vomiting, and abdominal pain as well as a variety of CNS and cardiovascular effects. The genus and species of the nutmeg tree is Myristica fragrans.

What are the toxicologically relevant components of nutmeg?

**Answer:**

Nutmeg contains 5-15% volatile oils, a mixture of alkyl benzene derivatives, terpenes and myristic acid. Myristicin, elemicin and saffrole make up 80% of the alkylbenzene derivatives. (Stein, et al. Nutmeg poisoning-report on a fatal case and a series of cases recorded by a poison information centre. 2001. Forensic Sci International 118:87-90)

**Wednesday, November 19, 2008****Question:**

Which form of solar UV radiation is capable of causing photoaging, skin cancer and immune suppression; UVA or UVB?

**Answer:**

Both UVA and UVB can cause photoaging, suppress immune function, and cause skin cancer (The Medical Letter. 50(1294), Sept, 2008)

**Tuesday, November 18, 2008****Question:**

True or False. Amoxicillin causes false-positive urine screens for cocaine metabolite.

**Answer:**

False. Although this is contended on various websites (www.alwaystestclean.com/false\_positive\_drug\_test.htm and others), the peer-reviewed medical literature does not support this. In one study of 33 subjects taking a course of amoxicillin, 31 tested negative for benzyldogonine on four common urine screening immunoassays. Two subjects tested positive by all four immunoassays and were confirmed to have benzyldogonine in the urine by GC-MS. So, amoxicillin only makes you test positive for cocaine if you are also taking cocaine.

Reisfield GM et al. Failure of amoxicillin to produce false-positive urine screens for cocaine metabolite. J Anal Toxicol. 2008 May;32(4):315-8.

**Monday, November 17, 2008****Question:**

Propylene glycol accumulation, as reflected by a hyperosmolar anion gap metabolic acidosis, may be observed in critically ill adults receiving continuous high-dose infusion of what drug for more than 48 hrs.

**Answer:**

Lorazepam (Arroliga et al. Relationship of continuous infusion of lorazepam to serum propylene glycol concentration in critically ill adults. 2004. Crit Care Med. 32(8):1709-1714)

**Friday, November 14, 2008****Question:**

The development of the hemolytic uremic syndrome has been reported to be associated with a variety of chemotherapeutic agents. Which chemotherapeutic agent is the most common cause of HUS?

**Answer:**

Mitomycin-C (Wu et al. Mitomycin-C induced hemolytic uremic syndrome: a case report and literature review. 1997. Jpn J Clin Oncol. 27(2): 115-118.

**Thursday, November 13, 2008****Question:**

What is the most serious complication of ingestion of Ginkgo biloba seeds, what is the compound responsible for this effect, and what is the recommended treatment?

**Answer:**

Seizures following ingestion of Ginkgo biloba seeds appear to be caused by 4-methoxypyridoxine (MPN) and should be treated by the administration of pyridoxal phosphate and a benzodiazepine such as diazepam. (Pediatrics, 2002 Feb, 109(2):325-7)

**Wednesday, November 12, 2008****Question:**

What are the poisonous constituents of horse chestnuts?

**Answer:**

Esculins in the saponin fraction of the horse chestnut. ( Bioorg Med Chem, 1999 Aug, 7(8):1737-41)

**Tuesday, November 11, 2008****Question:**

What ear malformations are typically seen in children whose mothers took isotretinoin during pregnancy?

**Answer:**

Partial duplications and tissue reductions and displacements. (Journal of Craniofacial Genetics & Developmental Biology, 1991 Oct-Dec, 11(4):292-5)

**Monday, November 10, 2008****Question:**

What is the most characteristic radiological finding in fetal warfarin syndrome?

**Answer:**

Epiphyseal stippling (J Med Assoc Thailand, 2005 Nov, 88 Suppl 8:S246-50)

**Friday, November 7, 2008****Question:**

True or False: Organs from patients dying from ingestion of poison hemlock can be transplanted safely.

**Answer:**

True. There is at least one case in which organs from a person who died from poison-hemlock poisoning were successfully transplanted. (Transplantation, 2003 Sep 15, 76(5):874-6)

**Thursday, November 6, 2008****Question:**

What are ways that fentanyl transdermal patches can be misused or abused?

**Answer:**

Therapeutic misuse can occur when patches are prescribed for mild or intermittent pain or in patients who are not opioid-tolerant; abuse can be in the form of chewing, injecting, or ingesting part or all of a patch, heating and then inhaling the contents of the patch, or applying patches to the skin or to the oral (buccal) or rectal mucosa. (Am J Emerg Med, 2002 Jan, 20(1):58-59)

**Wednesday, November 5, 2008****Question:**

What metal is being increasingly substituted for depleted uranium in military munitions, and how might it be more toxic than depleted uranium?

**Answer:**

False. Tungsten, which may pose a carcinogenic risk to a greater extent than does uranium. (Mil Med, 2007 Sep, 172(9):1002-5)

**Tuesday, November 4, 2008****Question:**

What is the predominant histopathological finding in the livers of patients who have died from poisonings from phosphide-containing pesticides?

**Answer:**

Fine cytoplasmic vacuolization (seen in almost 95% of fatalities). This vacuolization was distributed uniformly in all hepatic zones in 75% of cases. (Forensic Sci Int, 2007 Mar 2, 166(2-3):190-3)

<b>Monday, November 3, 2008</b>
<b>Question:</b> Acromelic acids are the probable etiologic agents of what disorder associated with consumption of mushrooms?
<b>Answer:</b> Erythromelalgia from Clitocybe mushrooms (Toxicological Reviews, 2006, 25(3):199-209)
<b>Friday, October 31, 2008</b>
<b>Question:</b> What is thought to be the composition of the chemical agent used by Russian Spetsnaz troops in the storming of the Moscow theater in which Chechyan rebels were holding hostages?
<b>Answer:</b> A potent fentanyl derivative (such as carfentanil) and an inhalational anesthetic (possibly halothane) (Ann Emerg Med, 2003, 41:700-705)
<b>Thursday, October 30, 2008</b>
<b>Question:</b> Name the most significant dose-dependent side effect of therapy with ethambutol.
<b>Answer:</b> Optic or retrobulbar neuritis may be seen with high-dose ethambutol therapy, typically only after 1.5 months. Dyschromatopsia is often the earliest indicator of toxicity, with blue-yellow color changes being the most common. (Melamud A et al. Ocular ethambutol toxicity. Mayo Clin Proc. 2003 Nov;78(11):1409-11)
<b>Wednesday, October 29, 2008</b>
<b>Question:</b> Name common medications responsible for phencyclidine false-positive results on urine drug screen immunoassays.
<b>Answer:</b> Common medications causing phencyclidine false-positives include dextromethorphan, diphenhydramine, ibuprofen, ketamine, meperidine, tramadol, venlafaxine, imipramine, and doxylamine. (Moeller KE, et al. Urine drug screening: practical guide for clinicians. Mayo Clin Proc. 2008 Jan;83(1):66-76)
<b>Tuesday, October 28, 2008</b>
<b>Question:</b> What is the metabolite responsible for hepatotoxicity in acute valproate overdose?
<b>Answer:</b> 4-en-VPA, a byproduct of omega oxidation, is the toxic metabolite that accumulates in acute valproate overdose once carnitine depletion occurs. 4-en-VPA is responsible for hyperammonemia seen in toxicity. (Lheureux PE et al. Science review: carnitine in the treatment of valproic acid-induced toxicity - what is the evidence? Crit Care. 2005 Oct 5;9(5):431-40)
<b>Monday, October 27, 2008</b>
<b>Question:</b> Name the King's College Criteria for acetaminophen-induced fulminant hepatic failure necessitating liver transplantation.
<b>Answer:</b> The criteria include a pH 100 seconds, creatinine >3.3 mg/dL, and grade III or IV encephalopathy. Since its inception, the additional criteria of a lactate >3.0 mmol after fluid resuscitation has come into use. (Makin AJ et al. A 7-year experience of severe acetaminophen-induced hepatotoxicity (1987-1993). Gastroenterol 1995;109:1907-1916.)
<b>Friday, October 24, 2008</b>
<b>Question:</b> Name medications implicated in drug-induced thrombotic thrombocytopenic purpura/hemolytic uremic syndrome.
<b>Answer:</b> This list is quite extensive, but can include ticlopidine, clopidogrel, ciprofloxacin, cephalixin, piperacillin, metronidazole, penicillin, famotidine, cimetidine, certain statins, antineoplastic agents, cyclosporine, tacrolimus, interferon, and quinidine. (Dlott JS et al. Drug-induced thrombotic thrombocytopenic purpura/hemolytic uremic syndrome: a concise review. Therapeutic Apheresis & Dialysis: Official Peer-Reviewed Journal of the International Society for Apheresis, the Japanese Society for Apheresis, the Japanese Society for Dialysis Therapy. 8(2):102-11, 2004 Apr.)
<b>Thursday, October 23, 2008</b>
<b>Question:</b> Describe the mechanism of wormwood toxicity.
<b>Answer:</b> Toxicity from wormwood (Artemisia absinthum) is due to its thujone components (both alpha- and beta-thujone). Alpha-thujone has been shown to bind and inhibit GABAA receptors, leading to convulsions. (Skyles AJ. Sweet BV. Wormwood. American Journal of Health-System Pharmacy. 61(3):239-42, 2004 Feb 1.)
<b>Wednesday, October 22, 2008</b>
<b>Question:</b> Describe signs and symptoms of camphor intoxication.
<b>Answer:</b> Camphor intoxication can involve nausea/vomiting, burning of the mouth/throat, and cyanosis of the lips in severe cases. Neurologic symptoms predominate, and include irritability, hyper-reflexia, tonic muscular contraction, myoclonic jerks, confusion, coma, and apnea. Seizures are common in significant intoxication and are often the presenting sign. (Love JN et al. Are one or two dangerous? Camphor exposure in toddlers. J Emerg Med. 2004 Jul;27(1):49-54)
<b>Tuesday, October 21, 2008</b>
<b>Question:</b> Describe the pathophysiology involving scorpion envenomation by Centroides exillicauda.
<b>Answer:</b> C. exillicauda venom consists of primarily neurotoxins causing sodium channel opening at neuromuscular junctions. Repetitive depolarization subsequently occurs in both the sympathetic and parasympathetic nervous system, causing simultaneous acetylcholine and catecholamine surges. (Rimsza ME et al. Scorpion envenomation. Pediatrics 1980;66:298-302)
<b>Monday, October 20, 2008</b>
<b>Question:</b> True or False: Lithium overdose can cause a low or negative anion gap?
<b>Answer:</b> True. This can be seen in toxicity due to the fact that lithium as a cation is not accounted for in the formula for calculating the anion gap. Other causes of a low or negative anion gap include bromide intoxication, nitrates, cationic immunoglobulins secondary to plasma cell dyscrasias, hypercalcemia, hypermagnesemia, and hyperkalemia. (Sood MM, Richardson R. Negative anion gap and elevated osmolar gap due to lithium overdose. CMAJ. 2007 Mar 27;176(7):921-3)
<b>Friday, October 17, 2008</b>



**Question:**

True or False: Patients concerned about mercury toxicity should have dental amalgams containing mercury removed?

**Answer:**

False. The process of removing dental amalgams generates mercury vapor with subsequent three to fourfold increase in blood mercury concentrations. (Molin M et al. Mercury, selenium, and glutathione peroxidase before and after amalgam removal in man. Acta Odontol Scand. 1990 Jun;48(3):189-202)

**Thursday, October 16, 2008**

**Question:**

Which of the following is the most salient finding in acute selenium salt overdose?

- A. Constipation
- B. Hair loss
- C. Hypotension
- D. Nail changes
- E. Seizure

**Answer:**

C. Refractory hypotension is thought to be caused by acute toxic cardiomyopathy and decreased peripheral vascular resistance. Hair loss and nail changes are associated with chronic overdose. Diarrhea, not constipation, may occur in acute or chronic overdoses. (Source: Hunsaker DM, Spiller HA, Williams D. Acute selenium poisoning: suicide by ingestion. J Forensic Sci. 2005 Jul;50(4):942-6.)

**Wednesday, October 15, 2008**

**Question:**

Amnesic shellfish poisoning is caused by which toxin?

- A. Brevetoxin
- B. Ciguatoxin
- C. Domoic acid
- D. Saxitoxin
- E. Tetrodotoxin

**Answer:**

C. Perl TM, Bedard L, Kosatsky T, Hockin JC, Todd EC, Remis RS. An outbreak of toxic encephalopathy caused by eating mussels contaminated with domoic acid. N Engl J Med. 1990 Jun 21;322(25):1775-80.

**Sunday, October 12, 2008**

**Question:**

Which of the following is not associated with benzonatate overdose?

- A. Tachycardia
- B. Agitation
- C. Seizure
- D. Ventricular dysrhythmia
- E. Hypertension

**Answer:**

E. Hypotension, not hypertension has been associated with benzonatate overdose. (Source: Spiller HA, Winter ML, Griffith JRK. Benzonatate ingestion reported to the national poison center database system. Clin Tox 46(7): 2008 p594.)

**Saturday, October 11, 2008**

**Question:**

True or False: Elevation of prothrombin time is an accurate indicator of acetaminophen induced hepatic failure.

**Answer:**

False. Administration of N-acetylcysteine (NAC) causes PT to be falsely elevated making interpretation of abnormal PT in patients on NAC protocols difficult. (Source: Lucena MI, Lopez-Torres E, Verge C, Andrade RJ, Puche MJ, Seoane J, de la Cuesta FS. The administration of N-acetylcysteine causes a decrease in prothrombin time in patients with paracetamol overdose but without evidence of liver impairment. Eur J Gastroenterol Hepatol. 2005 Jan;17(1):59-63.

**Friday, October 10, 2008**

**Question:**

Which of the following opioids produces the least miosis?

**Answer:**

B. Meperidine causes less miosis and duration of miosis is shorter. (Source: Ghoneim MM, Dhanaraj J, Choi WW. Comparison of four opioid analgesics as supplements to nitrous oxide anesthesia. Anesth Analg 1984 Apr;63(4):405-12.

**Thursday, October 9, 2008**

**Question:**

True or False?.. Sodium azide is responsible for facial and ocular injury due to automobile airbag deployment.

**Answer:**

False. An alkali aerosol containing sodium hydroxide and sodium carbonate is released into the passenger compartment of the car on airbag deployment. (Can Med J, 1995, 153(7):933-934)

**Wednesday, October 8, 2008**

**Question:**

Which drugs have been implicated in the development of diffuse alveolar hemorrhage (DAH) syndrome?

**Answer:**

Drugs used in the treatment of collagen vascular diseases, such as D-penicillamine reportedly can cause DAH. (Cleveland Clinic Journal of Medicine, 2008, 75(4): 258-280)

**Tuesday, October 7, 2008**

**Question:**

In May of 2006, the FDA issued a warning regarding the potential for the development of acute renal failure after the ingestion of a colonoscopy prep solution containing what substance?

**Answer:**

Sodium phosphate solution (NEJM, 2008, 359:9:951-960)