

AMERICAN ACADEMY OF CLINICAL TOXICOLOGY  
HERBS & DIETARY SUPPLEMENTS SPECIAL INTEREST GROUP  
ABSTRACTING SERVICE

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1. Maruyama Y, Hoshida S, Furukawa M, Ito M. Effects of Japanese herbal medicine, Juzen-taiho-to, in otitis-prone children--a preliminary study. *Acta Otolaryngol.* 2009;129(1):14-8. PMID: 18608005  
CONCLUSION: Juzen-taiho-to (JTT, TJ-48), a Japanese herbal medicine that improves immune function, was found to be effective in otitis-prone in children. OBJECTIVE: To evaluate the efficacy of JTT against intractable and recurrent infections in immature immune systems, we administered JTT to otitis-prone infants and investigated clinical changes before and during JTT administration. SUBJECTS AND METHODS: Twenty-four otitis-prone infants were administered JTT at 0.10-0.14 g/kg/day twice a day for 3 months. We compared clinical course, such as frequency of acute otitis media (AOM), duration of fever and antibiotics administration, and hospital visits for the periods before and during JTT administration. RESULTS: Medication compliance rate was 87.5%, and administration of JTT led to remission in 95.2% patients. No apparent side effects were observed. The frequency of AOM decreased significantly (Wilcoxon signed rank test,  $p=0.000$ ) with JTT. The duration of fever ( $p=0.000$ ) and administration of antibiotics ( $p=0.001$ ), as well as the number of hospital visits ( $p=0.001$ ) and emergent hospital visits ( $p=0.000$ ) showed significant decreases after JTT administration. After the end of the JTT period, 14 of 21 (66.7%) patients started to take it again, as they experienced purulent otitis media and/or other infections after discontinuation. The frequency of AOM increased significantly after stopping JTT ( $p=0.004$ ) and decreased again with JTT resumption ( $p=0.005$ ).
2. Woo TM. When nature and pharmacy collide: drug interactions with commonly used herbs. *Adv Nurse Pract.* 2008;16(7):69-72. PMID: 19181163
3. Low Dog T. The use of botanicals during pregnancy and lactation. *Altern Ther Health Med.* 2009;15(1):54-8. PMID: 19161049  
Women are the largest consumers of healthcare, and this extends to their utilization of complementary and alternative medicine (CAM). Researchers have attempted to uncover the reasons why women turn to CAM in general and to botanical medicine in particular. Desire to have personal control over their health has been cited as the strongest motive for women to use herbal medicine. Second was dissatisfaction with conventional treatment and its disregard for a holistic approach, as well as concerns about the side effects of medications.' These concerns may explain, in part, the fact that many women use herbal remedies during pregnancy. A survey of 578 pregnant women in the eastern United States reported that 45% of respondents had used herbal medicines, and a survey of 588 women in Australia revealed that 36% had used at least 1 herbal product during pregnancy. Women probably feel comfortable using herbal remedies because of their perceived safety, easy access, and the widespread availability of information about them (ie, Internet, magazines, books). While it is true that many botanicals are mild in both treatment effects and side effects, the data regarding safety during pregnancy are very limited. Given the small sample sizes in clinical trials studying botanicals in pregnant women, only large differences in measures of pregnancy outcomes would likely be detected. For example, if an herb were thought to increase the rate of spontaneous abortion from 6% to 7%, a sample size of more than 19000 women would be needed. It is highly unlikely that there will be any studies of a botanical (or drug) with this large a sample size. So when addressing the safety of an herb during pregnancy, we must look at the totality of the evidence, which includes traditional and contemporary use, animal studies, pharmacological studies, and clinical trial data, when available. Survey data tell us that women often do not share their use of herbal remedies with their healthcare providers due to fear of offending providers or to the belief that clinicians will be ignorant about their use. Practitioners should maintain an open and respectful demeanor when counseling pregnant and nursing women about the use of botanical medicines, and they should know how to access unbiased and authoritative information sources, so they may reliably answer questions on inadvertent exposures and provide guidance on herbal products that might be beneficial.
4. Teschke R, Schwarzenboeck A, Hennermann KH. Causality assessment in hepatotoxicity by

drugs and dietary supplements. *Br J Clin Pharmacol*. 2008;66(6):758-66. PMID: 19032721

Structured causality assessment of hepatotoxicity by drugs and dietary supplements (DDS) is a major clinical challenge, since temporal associations as the sole criteria for a valid evaluation are not acceptable. Initially, a clear intuition for an ad hoc evaluation is necessary, but only provisional, and must be followed by a diagnostic algorithm using a pretest, main test and post test. The evaluation is based on a variety of items such as latency period, course of alanine aminotransferase and alkaline phosphatase after DDS discontinuation, risk factors, co-medication, previous information on hepatotoxicity of the DDS, response to rechallenge, and exclusion of other diseases. It is essential that practising and hospital physicians as well as other key health professionals, such as pharmacists, gather all information required for a sound causality assessment, obviating major discussions by expert panels, manufacturers and health agencies in face of scanty and fragmentary data. Because pharmacogenetic alterations may trigger metabolic hepatotoxicity by a few DDS, levels in plasma and urine should be measured and may be helpful for diagnosis. Concomitant genotyping of cytochrome P450 and other enzymes may also be useful in future to minimize the risk of unwanted side-effects, including toxic liver disease elicited by DDS.

5. Chiang AP, Butte AJ. Data-driven methods to discover molecular determinants of serious adverse drug events. *Clin Pharmacol Ther*. 2009;85(3):259-68. PMID: 19177064

The dangers of serious adverse drug reactions (SADRs) are well known to clinicians, pharmacologists, and the lay public. Efforts to elucidate the molecular mechanisms behind SADRs have made significant progress through genetics and gene expression measurements. However, as the field of pharmacology adopts the same novel higher-density measurement modalities that have proven successful in other areas of biology, one wonders whether there can be more ways to benefit from the explosion of data created by these tools. The development of analytic tools and algorithms to interpret these biological data to create tools for medicine is central to the field of translational bioinformatics. In this review we introduce some of the types of SADR predictors that are required, and we discuss several databases that are publicly available for the study of SADRs, ranging from clinical to molecular measurements. We also describe recent examples of how bioinformatics methods coupled with data repositories can advance the science of SADRs.

6. Beyer NH, Kogutowska E, Hansen JJ, Engelhart Illigen KE, Heegaard NH. A mouse model for ricin poisoning and for evaluating protective effects of antiricin antibodies. *Clin Toxicol (Phila)*. 2009;47(3):219-25. PMID: 19274499

**BACKGROUND:** Ricin is a potential bioterrorism agent and no specific antidote or treatment exists for ricin poisoning. For this reason, we developed ricin-specific antibodies that were tested in a murine model of ricin poisoning for use as antidotes against symptoms of ricin poisoning. **METHODS:** Mice were poisoned with a lethal dose of ricin (5 microg) and their temperature and general condition were monitored for determination of a surrogate and humane end point. Mice were then treated with injections of ricin and different combinations of polyclonal anti-ricin antibodies. Antibody effect was evaluated for various doses and using various time points from ricin to antibody injection. Also, the effect of adjuvant symptomatic treatment was examined. Brain, heart, intestines, kidney, liver, lung, pancreas, spleen, and stomach tissues were sampled for histopathological analysis. **RESULTS:** The mouse model was reproducible and easy to use. A clear protective effect of both anti-ricin A-chain and anti-ricin B-chain antibodies-but not of irrelevant antibodies-was demonstrated with no added effect of symptomatic treatment. **CONCLUSIONS:** These data suggest that specific polyclonal antibodies against ricin A- and B-chain may reproducibly protect mice against ricin poisoning, even when the antibodies are administered up to 1.5 h after poisoning.

7. Kung SW, Chan YC, Tse ML, Lau FL, Chau TL, Tam MK. Acute renal failure and hepatitis following ingestion of carp gallbladder. *Clin Toxicol (Phila)*. 2008;46(8):753-7. PMID: 19238734

**INTRODUCTION:** Fish gallbladder has long been used as folk remedy in China. Poisoning due to carp gallbladder ingestion has been reported in many countries but the majority of cases are in Chinese journals. We report a case of grass carp gallbladder poisoning and review the literature, including the Chinese reports. **CASE REPORT:** A 67 year old woman ingested a grass carp gallbladder and complained of nausea and epigastric pain in two hours, and had elevated alanine aminotransferase by 8 hours. She developed oliguria on day three and hemodialysis was

performed on day five, following which she gradually recovered and was discharged on day 26. **DISCUSSION:** Carp gallbladder contains 5 alpha-cyprinol sulphate, which is hepatotoxic and nephrotoxic. The exact mechanism of toxicity is unknown. Mild poisoning causes only gastroenteritis, liver and kidneys are affected in moderate poisoning, and multi-organ failure occurs in severe poisoning. The initial symptoms are nausea, vomiting, diarrhea and abdominal pain, which usually occur 5 to 12 hours after ingestion. Raised liver enzymes or jaundice occurs in 75% to 87% of patients. Acute renal impairment occurs in 72% to 87% of patients, usually on day 3 to 6. Treatment is supportive and often included hemodialysis. **CONCLUSION:** The ingestion of grass carp gallbladder may result in transient hepatitis with subsequent acute renal failure. This case also illustrated the importance of understanding the use and potential serious complications of alternative medicines. Fish gallbladder poisoning should be considered in unexplained acute renal failure in Chinese and Asian patients.

8. Rajapakse S. Management of yellow oleander poisoning. *Clin Toxicol (Phila)*. 2009;47(3):206-12. PMID: 19306191  
**BACKGROUND:** Poisoning due to deliberate self-harm with the seeds of yellow oleander (*Thevetia peruviana*) results in significant morbidity and mortality each year in South Asia. Yellow oleander seeds contain highly toxic cardiac glycosides including thevetins A and B and nerifolin. A wide variety of bradyarrhythmias and tachyarrhythmias occur following ingestion. Important epidemiological and clinical differences exist between poisoning due to yellow oleander and digoxin; yellow oleander poisoning is commonly seen in younger patients without preexisting illness or comorbidity. Assessment and initial management. Initial assessment and management is similar to other poisonings. No definite criteria are available for risk stratification. Continuous ECG monitoring for at least 24 h is necessary to detect arrhythmias; longer monitoring is appropriate in patients with severe poisoning. Supportive care. Correction of dehydration with normal saline is necessary, and antiemetics are used to control severe vomiting. Electrolytes. Hypokalemia worsens toxicity due to digitalis glycosides, and hyperkalemia is life-threatening. Both must be corrected. Hyperkalemia is due to extracellular shift of potassium rather than an increase in total body potassium and is best treated with insulin-dextrose infusion. Intravenous calcium increases the risk of cardiac arrhythmias and is not recommended in treating hyperkalemia. Oral or rectal administration of sodium polystyrene sulfonate resin may result in hypokalemia when used together with digoxin-specific antibody fragments. Unlike digoxin toxicity, serum magnesium concentrations are less likely to be affected in yellow oleander poisoning. The effect of magnesium concentrations on toxicity and outcome is not known. Hypomagnesaemia should be corrected as it can worsen cardiac glycoside toxicity. Gastric decontamination. The place of emesis induction and gastric lavage has not been investigated, although they are used in practice. Gastric decontamination by the use of single dose and multiple doses of activated charcoal has been evaluated in two randomized controlled trials, with contradictory results. Methodological differences (severity of poisoning in recruited patients, duration of treatment, compliance) between the two trials, together with differences in mortality rates in control groups, have led to much controversy. No firm recommendation for or against the use of multiple doses of activated charcoal can be made at present, and further studies are needed. Single-dose activated charcoal is probably beneficial. Activated charcoal is clearly safe. Arrhythmia management. Bradyarrhythmias are commonly managed with atropine, isoprenaline, and temporary cardiac pacing in severe cases, although without trial evidence of survival benefit, or adequate evaluation of possible risks. Accelerating the heart rate with atropine or beta-adrenergic agents theoretically increases the risk of tachyarrhythmias, and it has been claimed that atropine increases tachyarrhythmic deaths. Further studies are required. Tachyarrhythmias have a poor prognosis and are more difficult to treat. Lidocaine is the preferred antiarrhythmic; the role of intravenous magnesium is uncertain. Digoxin-specific antibody fragments. Digoxin-specific antibody fragments are effective in reverting life-threatening cardiac arrhythmias; prospective observational studies show a beneficial effect on mortality. High cost and lack of availability limit the widespread use of digoxin-specific antibody fragments in developing countries. **CONCLUSIONS:** Digoxin-specific antibody fragments remain the only proven therapy for yellow oleander poisoning. Further studies are needed to determine the place of activated charcoal, the benefits or risks of atropine and isoprenaline, the place and choice of antiarrhythmics, and the effect of intravenous magnesium in yellow oleander poisoning.
9. Sandilands EA, Bateman DN. Adverse reactions associated with acetylcysteine. *Clin Toxicol*

(Phila). 2009;47(2):81-8. PMID: 19280424

**INTRODUCTION:** Paracetamol (acetaminophen) is one of the most common agents deliberately ingested in self-poisoning episodes and a leading cause of acute liver failure in the western world. Acetylcysteine is widely acknowledged as the antidote of choice for paracetamol poisoning, but its use is not without risk. Adverse reactions, often leading to treatment delay, are frequently associated with both intravenous and oral acetylcysteine and are a common source of concern among treating physicians. **METHODS:** A systematic literature review investigating the incidence, clinical features, and mechanisms of adverse effects associated with acetylcysteine. **RESULTS:** A variety of adverse reactions to acetylcysteine have been described ranging from nausea to death, most of the latter due to incorrect dosing. The pattern of reactions differs with oral and intravenous dosing, but reported frequency is at least as high with oral as intravenous. The reactions to the intravenous preparation result in similar clinical features to true anaphylaxis, including rash, pruritus, angioedema, bronchospasm, and rarely hypotension, but are caused by nonimmunological mechanisms. The precise nature of this reaction remains unclear. Histamine now seems to be an important mediator of the response, and there is evidence of variability in patient susceptibility, with females, and those with a history of asthma or atopy are particularly susceptible. Quantity of paracetamol ingestion, measured through serum paracetamol concentration, is also important as higher paracetamol concentrations protect patients against anaphylactoid effects. Most anaphylactoid reactions occur at the start of acetylcysteine treatment when concentrations are highest. Acetylcysteine also affects clotting factor activity, and this affects the interpretation of minor disturbances in the International Normalized Ratio in the context of paracetamol overdose. **CONCLUSION:** This review discusses the incidence, clinical features, underlying pathophysiological mechanisms, and treatment of adverse reactions to acetylcysteine and identifies particular "at-risk" patient groups. Given the commonality of adverse reactions associated with acetylcysteine, it is important to ensure that any adverse event does not preclude patients from receiving maximal hepatic protection, particularly in the context of significant paracetamol ingestion. Further work on mechanisms should allow specific therapies to be developed.

10. Varlibas F, Delipoyraz I, Yuksel G, Filiz G, Tireli H, Gecim NO. Neurotoxicity following chronic intravenous use of "Russian cocktail". *Clin Toxicol (Phila)*. 2009;47(2):157-60. PMID: 18608260

**INTRODUCTION:** Recently, neurological abnormalities in methcathinone users have been attributed to manganese. We report similar toxicity in three patients following the use of a mixture similar to methcathinone: potassium permanganate, ephedrine, and aspirin. **CASE REPORTS:** Three teenagers (15 to 19 years old) presented with extrapyramidal abnormalities and movement disorders following chronic intravenous use of a mixture known as "Russian Cocktail". All three patients had multiple movement disorders. One patient had normal blood manganese concentration (<19 microg/L) and MRI. The other two had elevated blood manganese (2100 microg/L and 3176 microg/L) and MRIs showing bilateral symmetric hyperintensities on T1-weighted-images in the dentate nucleus, subcortical white substance of cerebellar hemisphere, globus pallidus, and putamen. Abstinence and treatment with EDTA, levodopa, and para-aminosalicylic acid was associated with decreasing blood manganese concentrations and subjective improvement, but no change in objective findings. **DISCUSSION:** The "Russian Cocktail" likely contains manganese as a result of the oxidation of ephedrine by potassium permanganate in water acidified by acetylsalicylic acid. We believe that manganese with the possible contribution of methcathinone caused the neurological impairments. **CONCLUSIONS:** Three toxic substances have been made into a mixture administered intravenously, similar to methcathinone. Our patients learned of this mixture, called "Russian Cocktail", from their friends. The toxicity from repeated use of this mixture is one of extrapyramidal abnormalities and movement disorders. Standard therapies were unsuccessful in reversing the clinical toxicity.

11. Jing Z, Yang X, Ismail KM, Chen X, Wu T. Chinese herbal medicine for premenstrual syndrome. *Cochrane Database Syst Rev*. 2009(1):CD006414. PMID: 19160284

**BACKGROUND:** Traditional Chinese herbal medicines are frequently used to treat premenstrual syndrome (PMS) in China. Until now, their efficacy has not been systematically reviewed. **OBJECTIVES:** To evaluate the effectiveness and safety of traditional Chinese herbal medicines in the treatment of women with premenstrual syndrome. **SEARCH STRATEGY:** We searched MEDLINE (January 1950 to December, 2007), EMBASE (January 1980 to December, 2007),

Chinese Biomedical Database (CBM) (January 1975 to December, 2007), China National Knowledge Infrastructure (CNKI) (January 1994 to December, 2007), and the VIP Database (January 1989 to December, 2007). SELECTION CRITERIA: Randomised controlled trials (RCTs) studying the efficacy of traditional Chinese herbal medicine(s) for treatment of the premenstrual syndrome were included. DATA COLLECTION AND ANALYSIS: Two review authors telephoned the original authors of the RCTs to confirm the randomisation procedure, extracted and analysed data from the trials that met the inclusion criteria. MAIN RESULTS: Two RCT considering 549 women were included. One trial which was identified to be of higher methodological quality demonstrated the therapeutic effectiveness of Jingqianping granule. The other study was considered of lower quality due to the inherent risk of various biases in it. Two studies showed statistically significant differences in elimination of symptoms in proliferative phase and premenstrual phase by taking Jingqianping granule than taking Xiaoyaowan (RR 3.50, 95% CI 1.74 to 7.06). Women treated by CIPHER decoction had a higher rate of recovery than those taking Co-vitamin B6 capsules (RR 48.99, 95% CI 3.06 to 783.99). AUTHORS' CONCLUSIONS: It is rare in PMS management that efficacy claims are substantiated by clinical trials. One of the identified trials was well designed and reported on the effectiveness of Jingqianping in the treatment of premenstrual syndrome Qiao 2002. However, currently there is insufficient evidence to support the use of Chinese herbal medicine for PMS and further, well controlled, trials are needed before any final conclusions could be drawn.

12. Shim M, Saab S. Severe hepatotoxicity due to Hydroxycut: a case report. *Dig Dis Sci*. 2009;54(2):406-8. PMID: 18661239
13. Lim H, Kim HJ, Cho YS. A case of ricin poisoning following ingestion of Korean castor bean. *Emerg Med J*. 2009;26(4):301-2. PMID: 19307402  
Ricin is a member of a group of protein toxins whose cytosolic target is the 28S rRNA of the 60S ribosomal subunit. It was recently introduced as a weapon of terrorism in some countries. There is little evidence about the mechanism, diagnosis and treatment of ricin poisoning. The case history is reported of a patient with ricin poisoning who presented with nausea and vomiting following ingestion of Korean castor bean.
14. Boucher O, Muckle G, Bastien CH. Prenatal exposure to polychlorinated biphenyls: a neuropsychologic analysis. *Environ Health Perspect*. 2009;117(1):7-16. PMID: 19165381  
OBJECTIVES: A large body of literature documents the effects of prenatal exposure to polychlorinated biphenyls (PCBs) on cognitive development of children. Despite this fact, no integrative synthesis has been published yet to identify the cognitive functions that are particularly affected. Our aim is to review this literature in an attempt to identify the cognitive profile associated with prenatal PCB exposure. DATA SOURCES: Studies were identified by searching the PubMed database for articles published before June 2008. We reviewed data from nine prospective longitudinal birth cohorts for different aspects of cognition. DATA EXTRACTION: Associations between indicators of prenatal PCB exposure and performance on cognitive tasks reported in the selected studies are summarized and classified as general cognitive abilities, verbal or visual-spatial skills, memory, attention, and executive functions. DATA SYNTHESIS: The most consistent effects observed across studies are impaired executive functioning related to increased prenatal PCB exposure. Negative effects on processing speed, verbal abilities, and visual recognition memory are also reported by most studies. Converging results from different cohort studies in which exposure arises from different sources make it unlikely that co-exposure with another associated contaminant is responsible for the observed effects. CONCLUSION: Prenatal PCB exposure appears to be related to a relatively specific cognitive profile of impairments. Failure to assess functions that are specifically impaired may explain the absence of effects found in some studies. Our findings have implications in the selection of cognitive assessment methods in future studies.
15. Noah N. Food poisoning from raw fruit and vegetables. Introduction. *Epidemiol Infect*. 2009;137(3):305-6. PMID: 19274846
16. Li XM, Brown L. Efficacy and mechanisms of action of traditional Chinese medicines for treating asthma and allergy. *J Allergy Clin Immunol*. 2009;123(2):297-306; quiz 307-8. PMID: 19203653  
BACKGROUND: Although corticosteroids and beta(2)-agonists are effective in managing

asthma symptoms, a curative therapy for asthma is lacking. Traditional Chinese medicine (TCM), used in Asia for centuries, is beginning to play a role in Western health care as a complementary and alternative medicine modality. There is increasing scientific evidence supporting the use of TCM for asthma treatment. **OBJECTIVE:** This review article discusses promising TCM interventions for asthma and explores their possible mechanisms of action. **METHODS:** We first reviewed 5 clinical studies of antiasthma TCM herbal remedies published between 2005 and 2007. We then summarized possible mechanisms underlying their effects on the basis of data in the original articles, published abstracts, and available databases. Possible mechanisms include anti-inflammation, inhibition of airway smooth muscle contraction, and immunomodulation. Research on TCM herbal therapy for food allergy is rare, and we therefore focused on the effect and mechanism of action of food allergy herbal formula-2 on a murine model of peanut allergy and preliminary clinical study results. **CONCLUSION:** Evidence from clinical studies supports beneficial effects of TCM herbal therapy on asthma. A number of mechanisms may be responsible for efficacy of these agents. Strong preclinical study data suggest the potential efficacy of food allergy herbal formula-2 for food allergy.

17. Sicherer SH, Leung DY. Advances in allergic skin disease, anaphylaxis, and hypersensitivity reactions to foods, drugs, and insects in 2008. *J Allergy Clin Immunol.* 2009;123(2):319-27. PMID: 19203656

This review highlights some of the research advances in anaphylaxis, and hypersensitivity reactions to foods, drugs, and insects and in allergic skin disease that were reported in the Journal in 2008. Key epidemiologic observations include a rise in anaphylaxis in a population-based study and lower rates of peanut allergy in Israel, where infants consume peanut early compared with the United Kingdom, where dietary introduction is generally delayed. Advances in food allergy diagnosis include IgE epitope mapping that discloses the likelihood and severity of allergy; studies correlating likelihood of clinical reactivity on the basis of food-specific IgE to sesame, peanut, milk, and tree nuts; and an observation that a low baseline angiotensin-converting enzyme level may be associated with having pharyngeal edema during a reaction. Molecular, immunologic, and genetic studies are discerning pathways that are key in development of food allergy, identifying new modalities to interrupt mast cell degranulation, and elucidating risks associated with penicillin allergy. Regarding treatment, clinical studies show a majority of children with milk and egg allergy tolerate these proteins in modest amounts when they are extensively heated in baked goods, and studies show promise for oral immunotherapy to treat milk allergy and sublingual immunotherapy for honey bee venom hypersensitivity. The importance of skin barrier dysfunction has continued to be highlighted in the pathophysiology of atopic dermatitis (AD). Research has also continued to identify immunologic defects that contribute to the propensity of patients with AD to develop viral and bacterial infection. New therapeutic approaches to AD, urticaria, and angioedema have been reported including use of probiotics, biologics, vitamin D, and skin barrier creams.

18. Lai CK, Chan YW. Confirmation of gelsemium poisoning by targeted analysis of toxic gelsemium alkaloids in urine. *J Anal Toxicol.* 2009;33(1):56-61. PMID: 19161670

The gelsemium plants are highly poisonous but toxicological evaluation of suspected poisoning cases has been hampered by the chemical complexity of the gelsemium toxins involved. A novel liquid chromatography-tandem mass spectrometry protocol was optimized for the collective detection of gelsemine and related alkaloids from *Gelsemium elegans*. The screening protocol was applied to the clinical investigation of unexplained intoxications following the ingestion of seemingly nontoxic herbs. In three clusters of toxicological emergencies ranging from severe dizziness to respiratory failure, *Gelsemium elegans* mistaken for various look-alike therapeutic herbs was suspected to be the hidden cause of poisoning. Nine cases of gelsemium poisonings were thus ascertained by the diagnostic urine alkaloid profiles. Gelsemine was sustained as the main urinary marker of *Gelsemium* exposure.

19. Pillay VV. Current views on antidotal therapy in managing cases of poisoning and overdose. *J Assoc Physicians India.* 2008;56(881-92). PMID: 19263688

While it is an acknowledged dictum that in poisoning or overdose cases, the emphasis must be on general management comprising supportive measures than the use of specific antidotes in the vast majority of cases, it is nevertheless true that there are some instances where the timely use of a specific antidote or antagonist will dramatically reverse or at least halt the progression of toxicity. For this reason, and also because the indications and the exact manner in which

antidotes must be used could be controversial or unfamiliar to the physician, an attempt has been made to review the current concepts on antidotal therapy of poisoning. There is enough evidence that the proper use of specific antidotes when combined with general supportive care does reduce the morbidity and mortality associated with severe poisonings. Common antidotes used in a hospital setting have been discussed in some detail.

20. Barillo DJ. Diagnosis and treatment of cyanide toxicity. *J Burn Care Res.* 2009;30(1):148-52. PMID: 19060738
21. Eizadi-Mood N, Saghaei M, Alfred S, Zargarzadeh AH, Huynh C, Gheshlaghi F, Yaraghi A, Saad YS. Comparative evaluation of Glasgow Coma Score and gag reflex in predicting aspiration pneumonitis in acute poisoning. *J Crit Care.* 2009. PMID: 19327309  
PURPOSE: The purpose of the study was to assess the incidence of aspiration pneumonitis (AP) and its association with gag reflex and Glasgow Coma Score (GCS). MATERIALS AND METHODS: In a retrospective analysis study after prospective data collection, 155 poisoned patients with GCS less than or equal to 12 were evaluated. An assessment of GCS and the quality of gag reflex was made on arrival and recorded. Intubation status before gastrointestinal decontamination was noted. All patients were subsequently followed for developing of AP. RESULTS: The incidence of AP was 15.5%, with significant variance among patients with respect to the gag reflex, GCS, and the performance of intubation. A logistic regression model for predicting AP contained the following predictors: GCS (odds ratio [OR], 0.43; 95% confidence interval [CI], 0.30-0.62), intubation (OR, 0.07; 95% CI, 0.01-0.49), organophosphate ingestion (OR, 1.39; 95% CI, 0.96-2.01), and gastric evacuation (OR, 4.29; 95% CI, 0.94-9.51). In patients with reduced gag reflex, variations in GCS were associated with AP (OR, 0.43; 95% CI, 0.20-0.90), whereas in patients with absent gag reflex, age was the most important predictor of AP (OR, 2.67; 95% CI, 0.99-7.22). CONCLUSIONS: A reduced GCS and a nonintubated trachea are associated with an increased incidence of AP.
22. Schneider S, Diederich N, Appenzeller B, Schartz A, Lorang C, Wennig R. Internet suicide guidelines: report of a life-threatening poisoning using tobacco extract. *J Emerg Med.* 2009. PMID: 19272738  
Background: Severe nicotine intoxication occurred in a patient after ingestion of a tobacco extract made from a recipe found on a freely available Internet site. Objectives: To determine the levels of nicotine and cotinine in the plasma of a patient who tried to commit suicide by drinking a highly concentrated tobacco extract. Case report: A 67-year-old man tried to commit suicide by following guidelines found on an Internet site. He soaked 300 grams of tobacco for 3 days in water, evaporated most of the extract, and drank the rest of it. He felt sick immediately, with the following signs: respiratory depression, hypothermia, hypersalivation, bradycardia, and myoclonic jerks. Soon after the ingestion he vomited most of the extract. Toxicological analysis revealed potentially life-threatening nicotine and cotinine serum concentrations. Surprisingly, nicotine peak levels (322 mug/L) and cotinine peak levels (9092 mug/L) were reached more than 3 h after ingestion of the extract. Estimated nicotine and cotinine half-lives were 200 min and 1185 min, respectively. Treatment consisted of gastric lavage, ventilation, and monitoring of vital functions. The patient recovered and was discharged from the Emergency Department 4 days later without sequelae. Conclusion: Nicotinic intoxication is not always easy to recognize, and without clues from the patient and the toxicologic analysis, might well have been missed in the present case.
23. Brown RW, Longoria T. Multiple Risk Factors for Lead Poisoning in Hispanic Sub-Populations: A Review. *J Immigr Minor Health.* 2009. PMID: 19330449  
As a result of recent media attention to lead (Pb) in consumer products, Pb exposure and toxicity to children has been placed back on the national agenda. This review presents the current literature on sources of Pb in Hispanic sub-populations in the broader context of national lead poisoning trends, sources, and exposure pathways. Pb poisoning among Hispanics is a multi-dimensional issue that is far more complex than for the general population in terms of environmental, cultural, and social dimensions. As a result, a higher percentage of Hispanic children have elevated blood lead levels compared to the general population. Given the additional risks that Hispanics face, all Hispanic children should be defined as "at risk" for lead exposure and included in targeted screening programs. This review concludes with specific public policy recommendations that directly address the increased risk of Pb poisoning to

Hispanic children so that Pb will poison fewer children in the future.

24. Zorrilla P, Morales C, Gomez LA, Salido JA. Intravenous and subcutaneous injection of mercury: an unusual self-injury. *J Trauma*. 2009;66(3):E32-3. PMID: 18277286
25. Berger AJ, Alford K. Cardiac arrest in a young man following excess consumption of caffeinated "energy drinks". *Med J Aust*. 2009;190(1):41-3. PMID: 19120009  
An otherwise healthy 28-year-old man had a cardiac arrest after a day of motocross racing. He had consumed excessive amounts of a caffeinated "energy drink" throughout the day. We postulate that a combination of excessive ingestion of caffeine- and taurine-containing energy drinks and strenuous physical activity can produce myocardial ischaemia by inducing coronary vasospasm.
26. Ellis RJ, Toperoff W, Vaida F, van den Brande G, Gonzales J, Gouaux B, Bentley H, Atkinson JH. Smoked medicinal cannabis for neuropathic pain in HIV: a randomized, crossover clinical trial. *Neuropsychopharmacology*. 2009;34(3):672-80. PMID: 18688212  
Despite management with opioids and other pain modifying therapies, neuropathic pain continues to reduce the quality of life and daily functioning in HIV-infected individuals. Cannabinoid receptors in the central and peripheral nervous systems have been shown to modulate pain perception. We conducted a clinical trial to assess the impact of smoked cannabis on neuropathic pain in HIV. This was a phase II, double-blind, placebo-controlled, crossover trial of analgesia with smoked cannabis in HIV-associated distal sensory predominant polyneuropathy (DSPN). Eligible subjects had neuropathic pain refractory to at least two previous analgesic classes; they continued on their prestudy analgesic regimens throughout the trial. Regulatory considerations dictated that subjects smoke under direct observation in a hospital setting. Treatments were placebo and active cannabis ranging in potency between 1 and 8% Delta-9-tetrahydrocannabinol, four times daily for 5 consecutive days during each of 2 treatment weeks, separated by a 2-week washout. The primary outcome was change in pain intensity as measured by the Descriptor Differential Scale (DDS) from a pretreatment baseline to the end of each treatment week. Secondary measures included assessments of mood and daily functioning. Of 127 volunteers screened, 34 eligible subjects enrolled and 28 completed both cannabis and placebo treatments. Among the completers, pain relief was greater with cannabis than placebo (median difference in DDS pain intensity change, 3.3 points, effect size=0.60; p=0.016). The proportions of subjects achieving at least 30% pain relief with cannabis versus placebo were 0.46 (95%CI 0.28, 0.65) and 0.18 (0.03, 0.32). Mood and daily functioning improved to a similar extent during both treatment periods. Although most side effects were mild and self-limited, two subjects experienced treatment-limiting toxicities. Smoked cannabis was generally well tolerated and effective when added to concomitant analgesic therapy in patients with medically refractory pain due to HIV DSPN.
27. Luzi S, Morrison PD, Powell J, di Forti M, Murray RM. What is the mechanism whereby cannabis use increases risk of psychosis? *Neurotox Res*. 2008;14(2-3):105-12. PMID: 19073418  
Cannabis use has increased greatly over the last three decades. The various types of cannabis differ in their concentration of the main psychoactive component, Delta-9-tetrahydrocannabinol (THC), and the other major ingredient, cannabidiol (CBD). Plant engineering has maximized levels of THC, thus increasing the potency of street cannabis. It is well known that cannabis intoxication can cause brief psychotic symptoms like paranoia, whilst recent evidence demonstrates that heavy use of cannabis increases the risk of chronic psychoses like schizophrenia; genetic vulnerability seems to predispose some people to a higher risk. This paper starts to consider the neurochemical mechanisms whereby cannabis use increases the risk of psychosis.
28. Wiebe TH, Sigurdson ES, Katz LY. Angel's Trumpet (*Datura stramonium*) poisoning and delirium in adolescents in Winnipeg, Manitoba: Summer 2006. *Paediatr Child Health*. 2008;13(3):193-6. PMID: 19252697  
Over the course of the summer of 2006, four adolescent patients were hospitalized because of intentional *Datura stramonium* (Angel's Trumpet) ingestion. Their records were reviewed for the presence of signs and symptoms of toxicity, clinical course, treatment and outcome. All four patients had a decreased level of consciousness measured by the Glasgow Coma Scale, visual hallucinations, dilated pupils and agitation. The changes in mental status are characteristic of

delirium. All four patients were known to abuse substances. The average length of hospitalization was two days. No serious complications were encountered during hospitalization and a full recovery was noted in all patients. The use of sedation and restraints were sufficient treatment modalities. Health care workers should consider anticholinergic plant ingestion as a cause for abrupt onset of delirium.

29. Claudet I, Marechal C. Status epilepticus in a pediatric patient with amantadine overdose. *Pediatr Neurol.* 2009;40(2):120-2. PMID: 19135627  
A 2-year-old boy who ingested 0.8-1.5 g of amantadine developed status epilepticus. One hour later, the child presented with agitation, diaphoresis, and vomiting. He was admitted to the pediatric emergency department 2 hours later. Generalized seizures evolved to status epilepticus, with alternating generalized tonic-clonic and partial seizures, over a period of 7 hours. Other initial clinical signs were sinus tachycardia and reactive bilateral mydriasis. All symptoms resolved within 20 hours, with a good recovery; the child was released from the hospital on day 3.
30. Jones RL, Homa DM, Meyer PA, Brody DJ, Caldwell KL, Pirkle JL, Brown MJ. Trends in blood lead levels and blood lead testing among US children aged 1 to 5 years, 1988-2004. *Pediatrics.* 2009;123(3):e376-85. PMID: 19254973  
OBJECTIVES: To evaluate trends in children's blood lead levels and the extent of blood lead testing of children at risk for lead poisoning from national surveys conducted during a 16-year period in the United States. METHODS: Data for children aged 1 to 5 years from the National Health and Nutrition Examination Survey III Phase I, 1988-1991, and Phase II, 1991-1994 were compared to data from the survey period 1999-2004. RESULTS: The prevalence of elevated blood lead levels,  $\geq 10$  microg/dL, among children decreased from 8.6% in 1988-1991 to 1.4% in 1999-2004, which is an 84% decline. From 1988-1991 and 1999-2004, children's geometric mean blood lead levels declined in non-Hispanic black (5.2-2.8 microg/dL), Mexican American (3.9-1.9 microg/dL), and non-Hispanic white children (3.1 microg/dL to 1.7 microg/dL). However, levels continue to be highest among non-Hispanic black children relative to Mexican American and non-Hispanic white children. Blood lead levels were distributed as follows: 14.0% were  $< 1.0$  microg/dL, 55.0% were 1.0 to  $< 2.5$  microg/dL, 23.6% were 2.5 to  $< 5$  microg/dL, 4.5% were 5 to  $< 7.5$  microg/dL, 1.5% were 7.5 to  $< 10$  microg/dL, and 1.4% were  $\geq 10$  microg/dL. Multivariable analysis indicated that residence in older housing, poverty, age, and being non-Hispanic black are still major risk factors for higher lead levels. Blood lead testing of Medicaid-enrolled children increased to 41.9% from 19.2% in 1988-1991. Only 43.0% of children with elevated blood lead levels had previously been tested. CONCLUSIONS: Children's blood lead levels continue to decline in the United States, even in historically high-risk groups for lead poisoning. To maintain progress made and eliminate remaining disparities, efforts must continue to test children at high risk for lead poisoning, and identify and control sources of lead. Coordinated prevention strategies at national, state, and local levels will help achieve the goal of elimination of elevated blood lead levels.
31. Diez S. Human health effects of methylmercury exposure. *Rev Environ Contam Toxicol.* 2009;198(111-32. PMID: 19253038  
Mercury (Hg), and the organometallic compounds formed from it, are among the most toxic of substances to the global environment. Mercury is environmentally ubiquitous, and both wildlife and humans are exposed to the toxic effects of its environmental residues, primarily elemental mercury (Hg<sup>0</sup>), divalent mercury (Hg<sup>2+</sup>) and methylmercury (MeHg). Humans are exposed to different forms of Hg, and potential health risks have been reported from such exposures; examples of Hg exposure include mercury vapor from dental amalgams, occupational exposures and exposures during artisan and small-scale gold mining operations. Despite the significance of those foregoing Hg exposures, of particular concern is human and wildlife exposure to MeHg, a potent neurotoxicant. Once incorporated into the body, MeHg easily penetrates the blood-brain barrier and causes damage to the central nervous system, particularly in fetuses. It bioaccumulates and biomagnifies in the aquatic food chain; consequently, fish and seafood consumption is the major pathway by which humans are exposed to MeHg. MeHg is the focus of this review. It adversely affects humans and is currently the subject of intense public health interest and worldwide concern. In this review, I summarize the sources and cycling of global mercury in the environment, pathways of exposure, toxicity and exposure evaluation, toxicokinetics, the common biomarkers to evaluate exposure and effects in populations, and

finally review the nutritional risks and benefits from fish consumption.

32. Pillai U, Muzaffar J, Sen S, Yancey A. Grapefruit juice and verapamil: a toxic cocktail. *South Med J*. 2009;102(3):308-9. PMID: 19204629  
The US public consumes grapefruit juice in large quantities, with 14% of the population drinking the juice at least weekly. Grapefruit juice is a well-documented inhibitor of the CYP3A4 isoenzyme, which is involved in the metabolism of over 50% of commonly prescribed drugs. Here we report an unusual case of verapamil toxicity in a 42-year-old female, which resulted from accidental ingestion of only three tablets of the sustained release preparation (120 mg each) over 24 hours which resulted in severe toxicity.
33. Cordero MD, Moreno-Fernandez AM, Gomez-Skarmeta JL, de Miguel M, Garrido-Maraver J, Oropesa-Avila M, Rodriguez-Hernandez A, Navas P, Sanchez-Alcazar JA. Coenzyme Q10 and alpha-tocopherol protect against amitriptyline toxicity. *Toxicol Appl Pharmacol*. 2009;235(3):329-37. PMID: 19263520  
Since amitriptyline is a very frequently prescribed antidepressant drug, it is not surprising that amitriptyline toxicity is relatively common. Amitriptyline toxic systemic effects include cardiovascular, autonomous nervous, and central nervous systems. To understand the mechanisms of amitriptyline toxicity we studied the cytotoxic effects of amitriptyline treatment on cultured primary human fibroblasts and zebrafish embryos, and the protective role of coenzyme Q(10) and alpha-tocopherol, two membrane antioxidants. We found that amitriptyline treatment induced oxidative stress and mitochondrial dysfunction in primary human fibroblasts. Mitochondrial dysfunction in amitriptyline treatment was characterized by reduced expression levels of mitochondrial proteins and coenzyme Q(10), decreased NADH:cytochrome c reductase activity, and a drop in mitochondrial membrane potential. Moreover, and as a consequence of these toxic effects, amitriptyline treatment induced a significant increase in apoptotic cell death activating mitochondrial permeability transition. Coenzyme Q(10) and alpha-tocopherol supplementation attenuated ROS production, lipid peroxidation, mitochondrial dysfunction, and cell death, suggesting that oxidative stress affecting cell membrane components is involved in amitriptyline cytotoxicity. Furthermore, amitriptyline-dependent toxicity and antioxidant protection were also evaluated in zebrafish embryos, a well established vertebrate model to study developmental toxicity. Amitriptyline significantly increased embryonic cell death and apoptosis rate, and both antioxidants provided a significant protection against amitriptyline embryotoxicity.
34. States JC, Srivastava S, Chen Y, Barchowsky A. Arsenic and cardiovascular disease. *Toxicol Sci*. 2009;107(2):312-23. PMID: 19015167  
Chronic arsenic exposure is a worldwide health problem. Although arsenic-induced cancer has been widely studied, comparatively little attention has been paid to arsenic-induced vascular disease. Epidemiological studies have shown that chronic arsenic exposure is associated with increased morbidity and mortality from cardiovascular disease. In addition, studies suggest that susceptibility to arsenic-induced vascular disease may be modified by nutritional factors in addition to genetic factors. Recently, animal models for arsenic-induced atherosclerosis and liver sinusoidal endothelial cell dysfunction have been developed. Initial studies in these models show that arsenic exposure accelerates and exacerbates atherosclerosis in apolipoprotein E-knockout mice. Microarray studies of liver mRNA and micro-RNA abundance in mice exposed in utero suggest that a permanent state of stress is induced by the arsenic exposure. Furthermore, the livers of the arsenic-exposed mice have activated pathways involved in immune responses suggesting a pro-hyperinflammatory state. Arsenic exposure of mice after weaning shows a clear dose-response in the extent of disease exacerbation. In addition, increased inflammation in arterial wall is evident. In response to arsenic-stimulated oxidative signaling, liver sinusoidal endothelium differentiates into a continuous endothelium that limits nutrient exchange and waste elimination. Data suggest that nicotinamide adenine dinucleotide phosphate oxidase-derived superoxide or its derivatives are essential second messengers in the signaling pathway for arsenic-stimulated vessel remodeling. The recent findings provide future directions for research into the cardiovascular effects of arsenic exposure.
35. Inoue M, Lee N, Tsumuraya T, Fujii I, Hiramama M. Use of monoclonal antibodies as an effective strategy for treatment of ciguatera poisoning. *Toxicon*. 2009. PMID: 19254735  
Ciguatera is a global food poisoning caused by the consumption of fish that have accumulated

sodium channel activator toxins, ciguatoxins. At present, most diagnosed cases of ciguatera are treated with symptomatic and supportive remedies, and no specific therapy has been devised. Here we report that ciguatoxin CTX3C can be effectively neutralized in vitro and in vivo by simultaneous use of two anti-ciguatoxin monoclonal antibodies, providing the first rational approach toward directly preventing and treating ciguatera.

36. Warrell DA. Researching nature's venoms and poisons. *Trans R Soc Trop Med Hyg.* 2009. PMID: 19328509

Our environment hosts a vast diversity of venomous and poisonous animals and plants. Clinical toxinology is devoted to understanding, preventing and treating their effects in humans and domestic animals. In Sri Lanka, yellow oleander (*Thevetia peruviana*, Sinhala 'kaneru'), a widespread and accessible ornamental shrub, is a popular means of self-harm. Its toxic glycosides resemble those of foxglove, against which therapeutic antibodies have been raised. A randomised placebo-controlled trial proved that this treatment effectively reversed kaneru cardiotoxicity. There are strong scientific grounds for the use of activated charcoal, but encouraging results with multiple-dose activated charcoal were not confirmed by a recent more powerful study. Venom of Russell's viper (*Daboia siamensis*) in Burma (Myanmar) produces lethal effects in human victims. The case of a 17-year-old rice farmer is described with pathophysiological interpretations. During the first 9 days of hospital admission he suffered episodes of shock, coagulopathy, bleeding, acute renal failure, local tissue necrosis, generally increased capillary permeability and acute symptomatic hypoglycaemia with evidence of acute pituitary/adrenal insufficiency. Antivenom rapidly restored haemostatic function but failed to correct other effects of venom toxins incurred during the 3h before he could be treated.