

American Academy of Clinical Toxicology
Special Interest Group: Herbs & Dietary Supplements
Topic: Herbs, Ethnic Remedies, Dietary Supplements
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1. Abanades S, Farre M, Barral D, Torrens M, Closas N, Langohr K, Pastor A, de la Torre R. Relative abuse liability of gamma-hydroxybutyric acid, flunitrazepam, and ethanol in club drug users. *J Clin Psychopharmacol.* 2007;27(6):625-38. PMID: 18004131
OBJECTIVES: Despite the increasing concern about gamma-hydroxybutyric acid (GHB) toxicity, there are few studies examining the clinical pharmacology of GHB and its abuse potential. To evaluate GHB-induced subjective and physiological effects, its relative abuse liability and its impact on psychomotor performance in club drug users. MATERIALS AND METHODS: Twelve healthy male recreational users of GHB participated in 5 experimental sessions in the framework of a clinical trial. The study was randomized, double-blind, double-dummy, and crossover. Drug conditions were a single oral dose of GHB (40 or 60 mg/kg), ethanol (0.7 g/kg), flunitrazepam (1.25 mg), and placebo. Study variables included vital signs (blood pressure, heart rate, oral temperature, pupil diameter), psychomotor performance (digit symbol substitution test, balance, Maddox-Wing), subjective effects (a set of 13 visual analogue scales, Addiction Research Center Inventory-49 items, and Evaluation of the Subjective Effects of Substances with Potential of Abuse questionnaires), and pharmacokinetics. RESULTS: All active conditions induced positive effects related to their abuse potential. The administration of GHB produced euphoria and pleasurable effects with slightly higher ratings than those observed for flunitrazepam and ethanol. Gamma-hydroxybutyric acid induced a biphasic time profile with an initial stimulant-like effect related to the simultaneous rise of plasma concentrations and a latter sedative effect not related to GHB kinetics. Gamma-hydroxybutyric acid increased blood pressure and pupil diameter. Ethanol induced its prototypical effects, and flunitrazepam produced marked sedation. Gamma-hydroxybutyric acid and flunitrazepam impaired psychomotor performance, digit symbol substitution test, and balance task, whereas ethanol, at the dose tested, induced only mild effects exclusively affecting the balance task. CONCLUSIONS: Our results suggest a high abuse liability of GHB and flunitrazepam in club drug users.

2. Aberer W. Contact allergy and medicinal herbs. *J Dtsch Dermatol Ges.* 2008;6(1):15-24. PMID: 17919303
Herbal treatments are becoming increasingly popular, and are often used for internal as well as dermatological conditions, both externally as well as orally. The prevalence of contact sensitization against several plants especially of the Compositae family is quite high in Europe. Sensitization seems to occur relatively frequent with a few species such as arnica, elecampane and tea tree (oil), and occurs rarely with the majority. Testing for plant allergy is problematic because of the limited number of commercially available standardized patch test substances and the danger of active sensitization when testing with plants, parts thereof, or individual extracts. Knowledge about the allergic potential of plants is limited. Although plants are regarded as critical allergens by dermatologists, the number of reported cases of contact dermatitis is relatively small. Many widely used substances are not licensed as drugs or cosmetics. While the positive effects are frequently questionable or limited, the side effects are often more evident. Adverse effects of herbal medicines are an important albeit neglected subject in dermatology, which deserves further systematic investigation.

3. Algren DA. Management of the poisoned patient. *Mo Med.* 2008;105(1):47-52. PMID: 18300605
Poisoning is common and results in significant morbidity and mortality. The emergency physician should approach the evaluation and management of the poisoned patient with an unknown exposure in a stepwise fashion. Clues from the history, physical exam, and laboratory studies can often lead the emergency physician to the correct diagnosis. Gastrointestinal decontamination should not be

performed routinely and its use should be individualized in each patient. Poison centers and toxicologists can serve as a valuable resource in the management of the poisoned patient.

4. Baker JP. Mercury, vaccines, and autism: one controversy, three histories. *Am J Public Health*. 2008;98(2):244-53. PMID: 18172138
The controversy regarding the once widely used mercury-containing preservative thimerosal in childhood vaccines has raised many historical questions that have not been adequately explored. Why was this preservative incorporated in the first place? Was there any real evidence that it caused harm? And how did thimerosal become linked in the public mind to the "autism epidemic"? I examine the origins of the thimerosal controversy and their legacy for the debate that has followed. More specifically, I explore the parallel histories of three factors that converged to create the crisis: vaccine preservatives, mercury poisoning, and autism. An understanding of this history provides important lessons for physicians and policymakers seeking to preserve the public's trust in the nation's vaccine system.
5. Brown AC, Steensma DP, Tefferi A. The Possibility of Occult Lead Poisoning. *Mayo Clin Proc*. 2008;83(3):368. PMID: 18316006
No Abstract Available.
6. Cabb EE, Gorospe EC, Rothweiler AM, Gerstenberger SL. Toxic remedy: a case of a 3-year-old child with lead colic treated with lead monoxide (greta). *Clin Pediatr (Phila)*. 2008;47(1):77-9. PMID: 17693590
This article reports the case of a 3-year-old male with an elevated blood lead level. The child had a history of consuming imported lead-contaminated candies resulting in abdominal pains for which he was given a Hispanic folk remedy, called greta, by his mother. The home remedy aggravated the child's symptoms which prompted medical consultation. Analysis of the powdered folk remedy revealed a lead concentration of 140 000 ppm. This case highlights the complexities associated with identifying unfamiliar sources of lead poisoning, and their potential relationships to cultural practices.
7. Cahill SM, Wachsmuth IK, Costarrica Mde L, Ben Embarek PK. Powdered infant formula as a source of Salmonella infection in infants. *Clin Infect Dis*. 2008;46(2):268-73. PMID: 18171262
Powdered infant formula is not sterile and may be intrinsically contaminated with pathogens, such as *Salmonella enterica*, that can cause serious illness in infants. In recent years, at least 6 outbreaks of *Salmonella* infection in infants that have been linked to the consumption of powdered infant formula have been reported. Many of these outbreaks were identified because the *Salmonella* strains were unique in some way (e.g., a rare serotype) and a well-established *Salmonella* surveillance network, supported by laboratories capable of serotyping isolates, was in place. Another common feature of the outbreaks was the low level of salmonellae detected in the implicated formula (salmonellae may be missed in routine testing). These outbreaks likely represent only a small proportion of the actual number of *Salmonella* infections in infants that have been linked to powdered infant formula. Managing this problem requires a multidimensional approach in which manufacturers, regulators, and caregivers to infants can all play a role.
8. Caravati EM, Erdman AR, Christianson G, Nelson LS, Woolf AD, Booze LL, Cobaugh DJ, Chyka PA, Scharman EJ, et al. Elemental mercury exposure: an evidence-based consensus guideline for out-of-hospital management. *Clin Toxicol (Phila)*. 2008;46(1):1-21. PMID: 18167033
The objective of this guideline is to assist poison center personnel in the out-of-hospital triage and initial management of patients with suspected exposures to elemental mercury. An evidence-based expert consensus process was used to create this guideline. It is based on an assessment of current scientific and clinical information. The panel recognizes that specific patient care decisions may be at variance with this guideline and are the prerogative of the patient and health professionals

providing care. The grade of recommendation is in parentheses. Recommendations: 1) Patients with exposure due to suspected self-harm, abuse, misuse, or potentially malicious administration should be referred to an emergency department immediately regardless of the exposure reported (Grade D). 2) Patients with symptoms of acute elemental mercury poisoning (e.g., cough, dyspnea, chest pain) should be referred immediately to an emergency department for evaluation regardless of the reported dose. Patients with symptoms of chronic toxicity (rash, tremor, weight loss, etc.) should be referred for healthcare evaluation, the timing and location of which is guided by the severity of illness and circumstances of the exposure (Grade C). 3) If the elemental mercury was recently heated (e.g., from stove top, oven, furnace) in an enclosed area, all people within the exposure area should be evaluated at a healthcare facility due to the high risk of toxicity (Grade C). 4) If the elemental mercury was vacuumed or swept with a broom, the health department should be contacted to perform an environmental assessment for mercury contamination. Consider healthcare referral for those exposed to documented high air mercury concentrations (Grade C). 5) Patients ingesting more mercury than in a household fever thermometer or those with abdominal pain after ingestion should be referred to an emergency department for evaluation (Grade C). Do not induce emesis or administer activated charcoal. 6) Asymptomatic patients with brief, unintentional, low-dose vapor exposures can be observed at home. Asymptomatic patients can be evaluated as non-urgent outpatients if there is concern for exposures to high doses (e.g., more than contained in a thermometer) or for chronic duration (Grade D). 7) Pregnant patients unintentionally exposed to elemental mercury and who are asymptomatic should be evaluated by their obstetrician or primary care provider as an outpatient. Immediate referral to an ED is not required (Grade D). 8) Patients with elemental mercury deposited or injected into soft tissue should be referred for evaluation of surgical removal (Grade C). 9) All elemental mercury spills should be properly cleaned up, including the small amount of mercury from a broken thermometer. Brooms and vacuum cleaners should not be used to clean up elemental mercury. The clean-up of any spill larger than a broken thermometer should be performed by a professional company, state health department, or the EPA. Detailed instructions are provided on the EPA website: www.epa.gov/epaoswer/hazwaste/mercury/faq/spills.htm (Grade D). 10) Patients with dermal exposures should remove all jewelry and wash the affected area with mild soap and water. Remove all contaminated clothing and place these items in a sealed plastic double-bag for proper disposal (Grade D). 11) Do not discard elemental mercury in household trash, plumbing drains, or sewer systems. Consult local authorities for the proper disposal of low-level elemental mercury-contaminated household items and thermometers (Grade D).

9. de Medeiros LM, Fransway AF, Taylor JS, Wyman M, Janes J, Fowler JF, Jr., Rietschel RL. Complementary and alternative remedies: an additional source of potential systemic nickel exposure. *Contact Dermatitis*. 2008;58(2):97-100. PMID: 18186743
BACKGROUND: Systemic contact dermatitis from nickel has been reported from a number of sources including medical devices and following experimental oral exposure. OBJECTIVE: To identify other potential sources of systemic nickel exposure. METHODS: The internet and published medical literature were searched for complementary and alternative remedies which contain nickel. RESULTS: We identified and evaluated sources of nickel exposure in 4 homeopathic preparations, which are advertised to treat common skin diseases, as well as in a number of other homeopathic remedies, several herbal products and multivitamin mineral complexes. CONCLUSION: Complementary and alternative remedies are an additional source of systemic nickel exposure and at highest doses the potential risk for systemic contact dermatitis in nickel allergic patients should be considered.
10. Di Luigi L. Supplements and the endocrine system in athletes. *Clin Sports Med*. 2008;27(1):131-51, ix. PMID: 18206572
In the world of athletes' nutrition, there are many ethical concerns, because there is the suspicion that in practice, large doses of supplements in athletes are not taken for nutritional purposes. It is beyond the scope of this article to highlight the possible roles of supplements or methods of supplementation

in the improvement of athletic performance in elite athletes. Instead, the author briefly reviews some of the substances taken by athletes, with particular attention to their mechanisms of action and the pathways involved. Very often, the effects of many supplements are hormone-related, or supplements influence hormone secretion. Examples of possible links between "supplements or ergogenic compounds" and the endocrine/metabolic system are addressed.

11. Ellington L, Matwin S, Jasti S, Williamson J, Crouch B, Caravati M, Dudley W. Poison control center communication and impact on patient adherence. *Clin Toxicol (Phila)*. 2008;46(2):105-9. PMID: 18259957
Objective. This project explored the communication processes associated with poison control center calls. Methods. In this preliminary study, we adapted the Roter Interaction Analysis System to capture staff-caller dialogue. This involved case selection, wherein adherence and non-adherence cases were selected; call linkage to medical records, where case records were linked with voice recordings; and application of Roter Interaction Analysis System to calls. Results. Results indicate that communications are predominantly provider-driven. Patient age and percentage of staff partnership statements were significantly associated with adherence at the 0.05 level. Increases in age were associated with decreases in adherence to recommendations ($p < 0.001$). Increases in percentage of staff partnership statements (over all staff talk) were associated with increases in adherence ($p = 0.013$). Conclusion. This line of research could lead to evidence-based guidelines for effective staff-caller communication, increased adherence rates, and improved health outcomes.
12. Eyer P, Eyer F. Is this the epitaph for multiple-dose activated charcoal? *Lancet*. 2008;371(9612):538-9. PMID: 18280313
13. Feldman KW, Mazor S. Ecstasy ingestion causing heatstroke-like, multiorgan injury in a toddler. *Pediatr Emerg Care*. 2007;23(10):725-6. PMID: 18090107
3,4-Methylenedioxymethamphetamine (MDMA) ingestion can cause febrile status epilepticus in children but has not been reported to cause multiorgan dysfunction seen in young adults. We describe a toddler who was diagnosed at this stage of multiorgan injury. This drug, a synthetic amphetamine, has the "street" name of "ecstasy" and is commonly used by teenagers and young adults to augment the euphoric experience of "raves."
14. Flora SJ, Bhadauria S, Kannan GM, Singh N. Arsenic induced oxidative stress and the role of antioxidant supplementation during chelation: a review. *J Environ Biol*. 2007;28(2 Suppl):333-47. PMID: 17929749
Arsenic is a naturally occurring metalloid, ubiquitously present in the environment in both organic and inorganic forms. Arsenic contamination of groundwater in the West Bengal basin in India is unfolding as one of the worst natural geoenvironmental disaster to date. Chronic exposure of humans to high concentration of arsenic in drinking water is associated with skin lesions, peripheral vascular disease, hypertension, Blackfoot disease and high risk of cancer The underlying mechanism of toxicity includes the interaction with the sulphhydryl groups and the generation of reactive oxygen species leading to oxidative stress. Chelation therapy with chelating agents like British Anti Lewisite (BAL), sodium 2,3-dimercaptopropane 1-sulfonate (DMPS), meso 2,3 dimercaptosuccinic acid (DMSA) etc., is considered to be the best known treatment against arsenic poisoning. The treatment with these chelating agents however is compromised with certain serious drawbacks/side effects. The studies show that supplementation of antioxidants along with a chelating agent prove to be a better treatment regimen. This review attempts to provide the readers with a comprehensive account of recent developments in the research on arsenic poisoning particularly the role of oxidative stress/free radicals in the toxic manifestation, an update about the recent strategies for the treatment with chelating agents and a possible beneficial role of antioxidants supplementation to achieve the optimum effects.

15. Glassock RJ. Uremic toxins: what are they? An integrated overview of pathobiology and classification. *J Ren Nutr.* 2008;18(1):2-6. PMID: 18089436
Toxic substances, known as uremic toxins, accumulate in body fluids during the course of progressive, chronic kidney disease. This article will briefly summarize current views on the definition, physico-chemical characteristics, pathobiological mechanisms for generation and retention, and cellular pathophysiology of uremic toxins. In addition, this article will attempt to integrate these disparate phenomena into a systems biology approach as to how such toxins lead to the diverse clinical manifestations so characteristic of the uremic state.
16. Hanjani NM, Fender AB, Mercurio MG. Chronic arsenicism from Chinese herbal medicine. *Cutis.* 2007;80(4):305-8. PMID: 18038692
Chronic arsenicism is associated with cutaneous manifestations, including palmoplantar keratoses, pigmentary anomalies, and nonmelanoma skin cancer. It occurs most commonly following exposure to inorganic arsenic in contaminated drinking water or occupational contact, though medicinal exposure also has been reported. We present a case of a Chinese woman living in the United States with cutaneous manifestations of chronic arsenicism due to a 5-year history of Chinese herbal medicine ingestion.
17. Hersh EV, Pinto A, Moore PA. Adverse drug interactions involving common prescription and over-the-counter analgesic agents. *Clin Ther.* 2007;29 Suppl(2477-97. PMID: 18164916
BACKGROUND: Eight analgesic preparations with approved indications for acute pain were among the top 200 drugs prescribed in the United States in 2006. In addition, an estimated 36 million Americans use over-the-counter (OTC) analgesics daily. Given this volume of use, it is not surprising that a number of drug interactions involving analgesic drugs have been reported. OBJECTIVES: This article examines the pharmacologic factors that enhance the clinical relevance of potential drug interactions and reviews the literature on drug interactions involving the most commonly used analgesic preparations in the United States. METHODS: A PubMed search was conducted for English-language articles published between January 1967 and July 2007. Among the search terms were drug interactions, acetaminophen, aspirin, ibuprofen, naproxen, celecoxib, NSAIDs, hydrocodone, oxycodone, codeine, tramadol, OTC analgesics, alcohol, ethanol, antihypertensive drugs, methotrexate, warfarin, SSRIs, paroxetine, fluoxetine, sertraline, citalopram, serotonin syndrome, MAOIs, and overdose. Controlled clinical trials, case-control studies, and case reports were included in the review. RESULTS: A number of case reports and well-controlled clinical trials were identified that provided evidence of the relatively well known drug-drug interactions between prescription/OTC NSAIDs and alcohol, antihypertensive drugs, high-dose methotrexate, and lithium, as well as between frequently prescribed narcotics and other central nervous system depressants. In contrast, the ability of recent alcohol ingestion to exacerbate the hepatotoxic potential of therapeutic doses of acetaminophen is not supported by either case reports or clinical research. Use of ibuprofen according to OTC guidelines in patients taking cardioprotective doses of aspirin does not appear to interfere with aspirin's antiplatelet activity, whereas chronic prescription use of ibuprofen and other NSAIDs may interfere. Low-dose aspirin intake appears to abolish the gastroprotective effects of cyclooxygenase-2-selective inhibitors, including celecoxib. There is evidence of other less well known and potentially clinically significant drug-drug interactions, including the ability of selective serotonin reuptake inhibitors to inhibit the analgesic activity of tramadol and codeine through inhibition of their metabolic activation, to induce serotonin syndrome when used chronically in the presence of high doses of tramadol through synergistic serotonergic action, and to increase the potential for gastrointestinal bleeding associated with NSAID therapy through additive or supra-additive antiplatelet activity. CONCLUSIONS: Considering the widespread use of analgesic agents, the overall incidence of serious drug-drug interactions involving these agents has been relatively low. The most serious interactions usually involved other interacting drugs with low therapeutic indices or chronic and/or high-dose use of an analgesic and the interacting drug.

18. Kotsirilos V. -Hydroxybutyrate poisoning from toy beads. *Med J Aust.* 2008;188(5):316. PMID: 18312202
19. Krenzelok E, Mrvos R, Mazo E. Combining primary and secondary poison prevention in one initiative. *Clin Toxicol (Phila).* 2008;46(2):101-4. PMID: 18259956
Objective. Contrary to the recommendations of the Institute of Medicine (IOM) report on Forging a Poison Prevention and Control System, a certified regional poison information center combined both primary and secondary education with another public health initiative to determine if there was an impact on poison center awareness. Methods. Poison Help stickers that contained the national toll-free poison center number were inserted into a quarterly publication from a children's hospital and mailed to 136,741 residents of a poison center service region. Benchmark data from a six-month period were used to compare call volume both before and after the initiative. Results. Call volume increased by a mean of 8.8% from the counties where at least 5% of residents received the mailing. Conclusions. A single passive mass-mailing education program that combined primary and secondary poison prevention education may have had a small, but positive impact on poison center call volume when a threshold of 5% of the residents received the information.
20. Kristinsson J, Palsson R, Gudjonsdottir GA, Blondal M, Gudmundsson S, Snook CP. Acute poisonings in Iceland: A prospective nationwide study. *Clin Toxicol (Phila).* 2008;46(2):126-32. PMID: 18259960
Introduction. Poisoning is a common cause of emergency visits and hospital admission in Western countries. The purpose of this study was to assess the incidence and type of toxic exposures presenting to emergency medical facilities in Iceland. Materials and methods. The study was prospective and included all patients with confirmed or suspected poisoning presenting to hospitals and rural medical centers providing emergency services in Iceland during the twelve-month period from April 2001 until March 2002. Results. A total of 1,121 toxic exposures were documented representing an incidence of 3.91 cases per 1,000 inhabitants per year. The female to male ratio was 1.23. The majority of exposures (56.7%) occurred in the patient's home, 60% were deliberate, 72% had drugs and/or alcohol as their main cause, and 11% involved illicit drugs. Exposures to chemicals other than drugs were usually unintentional. Conclusion. Toxic exposures requiring emergency medical care are common in Iceland. Self-poisonings by ingestion of prescription drugs and/or alcohol accounted for the majority of cases.
21. Lancaster T, Stead L, Cahill K. An update on therapeutics for tobacco dependence. *Expert Opin Pharmacother.* 2008;9(1):15-22. PMID: 18076335
The aim of this review is to consider the clinical trial evidence for the efficacy of four classes of pharmacological treatment for nicotine dependence: nicotine replacement, antidepressants, nicotine-receptor partial agonists and drugs blocking cannabinoid receptors. Despite falls in many developed countries, the prevalence of smoking remains high and is increasing in developing countries. Stopping smoking before middle age substantially reduces the mortality associated with tobacco use. Although many people quit without formal help, both non-pharmacological and pharmacological interventions can help people to stop smoking. Drug therapies target neural pathways to reduce withdrawal symptoms associated with psychopharmacological dependence on nicotine. Nicotine replacement therapy and some antidepressants aid smoking cessation and are an established part of therapy. Newer pharmacological approaches include the use of the selective nicotinic partial agonists, varenicline and cytisine, and compounds targeting cannabinoid receptors (rimonabant). Recent evidence suggests that the nicotine-receptor partial agonist varenicline is at least as effective as nicotine replacement therapy and antidepressants.
22. Lane SD, Webster NJ, Levandowski BA, Rubinstein RA, Keefe RH, Wojtowycz MA, Cibula DA, Kingson JE, Aubry RH. Environmental injustice: childhood lead poisoning, teen pregnancy, and

tobacco. *J Adolesc Health*. 2008;42(1):43-9. PMID: 18155029

PURPOSE: This study investigates the persistent relationships between childhood lead exposure, repeat teen pregnancy, and tobacco use in a sample of teenage females in Syracuse, NY.

METHODS: We analyzed the association of childhood lead poisoning with repeat pregnancy and tobacco use among 536 teens (aged 15-19 years) in Syracuse, NY, who received services at Syracuse Healthy Start between 1998 and 2002. **RESULTS:** The mothers' childhood lead exposure, controlling for race, age, and Medicaid status, was associated with repeat teen pregnancy and tobacco use.

CONCLUSION: Long-term negative health outcomes associated with childhood lead exposure should not be underestimated. This study helps to shore up prior research that found lead poisoning to have a long-lasting impact on children's functioning and healthy development. Policy efforts focused on neighborhood development and health education continue to be sorely needed.

23. Levin P. From mad hatters to dental amalgams: heavy metals: toxicity and testing. *MLO Med Lab Obs*. 2007;39(12):20, 22, 24. PMID: 18236966

24. Levy A, Bailey B, Letarte A, Dupuis C, Lefebvre M. Unproven ingestion: an unrecognized bias in toxicological case series. *Clin Toxicol (Phila)*. 2007;45(8):946-9. PMID: 18163237

BACKGROUND: Case series of ingestion in preschool children may include patients without significant exposure if the substance is not measured. **METHODS:** In order to evaluate the unproven ingestion bias, we conducted, between January 2000 and June 2004, a retrospective analysis of a poison control center-based series of children <6 years old with a history of toxic methanol or ethylene glycol ingestion. **RESULTS:** Over the 54 month period, 115 children were referred to obtain a level. Of these, 102 children, aged 25 +/- 10 months, actually had a level analyzed. Only 21 patients had positive levels measured a median of 90 minutes post-ingestion. **CONCLUSION:** Our findings suggest that a significant fraction of purported cases were not confirmed. When a study aims at determining the toxicity of the substance, measurements of the xenobiotic should be required in any case series involving preschool aged children in order to decrease the unproven ingestion bias.

25. Mrvos R, Swanson-Biearman B, Krenzelok EP. Backyard mushroom ingestions: no gastrointestinal decontamination--no effect. *J Emerg Med*. 2007;33(4):381-3. PMID: 17976769

Treating the unintentional "backyard" mushroom ingestion continues to be controversial. A review of pediatric "backyard" mushroom ingestions was conducted. A Regional Poison Information Center (RPIC) conducted a retrospective review of all mushroom ingestions in children younger than 6 years of age. Data were extracted from the RPIC electronic record system for the years 2000-2003. All exposures that involved "backyard" mushroom ingestions with no gastrointestinal decontamination were included. There were 322 mushroom exposures in children younger than 6 years of age reviewed. The mean age reported was 2.1 years (SD +/- 1.18). All exposures with a definitive outcome had a 24-h follow-up post-exposure to make this determination. There was no effect in 256 cases (79.5%); minor effect in 6 (1.9%); judged as nontoxic, expect no effect in 20 (6.2%); minimal clinical effects possible in 31 (9.6%); and unrelated effect in 9 (2.8%). It was concluded that "backyard" mushrooms do not present a toxicity hazard in unintentional pediatric exposures and require no gastrointestinal decontamination.

26. Mydlik M, Derzsiova K. Oxalic Acid as a uremic toxin. *J Ren Nutr*. 2008;18(1):33-9. PMID: 18089441

OBJECTIVE: Oxalic acid (OA) is thought to be a uremic toxin that participates in the pathogenesis of uremic syndrome. The objectives of this study were to: (1) evaluate the plasma levels of OA in patients with chronic renal disease with various levels of glomerular filtration rate and after renal transplantation; (2) investigate the salivary secretion of OA and ascorbic acid in healthy subjects and in patients with chronic renal failure (CRF); (3) examine the influence of water and sodium diuresis and furosemide administration on the urinary excretion of OA and ascorbic acid in healthy subjects and in CRF patients without dialysis treatment; and (4) evaluate the influence of renal replacement

therapy (RRT) on secondary hyperoxalemia in hemodialysis patients. **DESIGN AND SETTING:** This study was conducted at the Nephrological Department of P.J. Safarik University. Sixty-one patients with chronic renal disease, 64 CRF patients, 32 continuous ambulatory peritoneal dialysis (CAPD) patients, 15 hemodialysis patients, 21 patients after renal transplantation, and 15 healthy subjects were examined. Maximal water diuresis, diets with low (2 g/day) and high (15 g/day) sodium intake, administration of intravenous furosemide (20 mg), and renal replacement therapy (CAPD, hemodialysis, hemofiltration, and postdilution hemodiafiltration) were utilized in the study. **RESULTS:** In patients with chronic renal disease and those after renal transplantation, direct relationships between plasma OA and serum creatinine were found ($r = 0.904$ and 0.9431 , respectively, $P < .01$). Despite a high level of plasma OA in uremic patients (23.1 ± 10 micromol/L), there was no significant difference in salivary OA between control subjects (128 ± 19 micromol/L) and CRF patients (135 ± 24 micromol/L). The urinary excretion of OA during maximal water diuresis (from 37.5 to 110.3 micromol/4 hours) and after intravenous furosemide (from 34.5 to 66.7 micromol/3 hours) increased significantly, but was not affected by high intake of NaCl. The most significant decrease of plasma OA was observed during postdilution hemodiafiltration (63.3%). **CONCLUSION:** Our study indicates that renal replacement therapy is not effective for a permanent reduction of elevated plasma levels of OA.

27. Pathak A, Mahmood A, Pathak R, Dhawan D. Effect of zinc on hepatic drug metabolism under ethanol toxicity. *Drug Chem Toxicol.* 2008;31(1):163-73. PMID: 18161515
The effects of zinc on drug-metabolizing enzymes in the liver were examined in male Wistar rats following ethanol intoxication. Rats were orally fed 3 mL of 30% ethanol daily for either two, four, or eight weeks and were orally administered zinc sulfate ($ZnSO_4 \cdot 7H_2O$) at a dose level of 227 mg/L. Levels of reduced glutathione (GSH) and the activities of cytochrome P-450, cytochrome b(5), NADPH cytochrome-C-reductase and glutathione-S-transferase (GST) were determined in liver after two, four, and eight weeks. Significant elevation was observed in the activities of the enzymes of the mixed function oxidase system in response to toxicity induced by ethanol at all the intervals. These effects were ascribed to the enhanced activity of the microsomal ethanol oxidizing system and the associated increase in reactive oxygen species production. Zinc supplementation to these ethanol-intoxicated animals resulted in normalization of these elevated values significantly, but still they do not attain normal levels. Significant increase was observed in reduced glutathione content in animals after four and eight weeks of ethanol feeding, which appeared to be further elevated in combined zinc and ethanol treatment. Significant elevation in the activity of GST was illustrated on ethanol-fed animals at all the three treatment intervals. Furthermore, the activity of this enzyme was only moderately normalized following zinc treatment. This was accredited to the antioxidant potential of zinc, as well as its ability to induce metallothionein content, which provide protection against the toxic effects of ethanol. To conclude, zinc was able to normalize the effects of ethanol in the liver.
28. Paulsen E, Chistensen LP, Andersen KE. Cosmetics and herbal remedies with Compositae plant extracts - are they tolerated by Compositae-allergic patients? *Contact Dermatitis.* 2008;58(1):15-23. PMID: 18154553
BACKGROUND: Compositae-sensitive patients are routinely warned against topical use of Compositae-containing cosmetics and herbal remedies. However, the risk of elicitation of dermatitis in presensitized persons is unknown. **OBJECTIVES:** The main aim of this study was to assess the significance of direct plant allergen contact via Compositae-derived cosmetics and herbal remedies in Compositae-allergic patients with special reference to arnica (*Arnica montana*) and German chamomile (*Chamomilla recutita*). **METHODS:** 8 of 12 chamomile-sensitive patients tested positive to chamomile-containing preparations, including tea, creams, ointments, and oil. 5 of 6 arnica-sensitive persons tested positive to arnica-based products. **RESULTS:** When the group was patch tested with cosmetic and/or herbal product ingredients, plant allergens elicited positive reactions most frequently, but fragrances, emulsifiers, and preservatives tested positive as well. Plant allergens were mainly derived from Compositae, but avocado oil, and *Hamamelis virginiana* tincture were

unexpectedly detected as sensitizers too. Chemical analyses indicated that the Compositae allergens were both sesquiterpene lactones and other naturally occurring compounds. CONCLUSION: In conclusion, Compositae-allergic persons should be warned against topical use of Compositae-containing products, not only because of the plant allergens, but also because of allergenic cream constituents that may cause reactions in the group of patients who have multiple contact allergies beside the Compositae allergy.

29. Pullela R, Young L, Gallagher B, Avis SP, Randell EW. A Case of Fatal Aconitine Poisoning by Monkshood Ingestion. *J Forensic Sci.* 2008. PMID: 18284527
Accidental aconitine poisoning is extremely rare in North America. This report describes the confirmation of a case of accidental aconitine poisoning using a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method. The case involved a 25-year-old man who died suddenly following a recreational outing with friends where he consumed a number of wild berries and plants including one that was later identified as Monkshood (*Aconitum napellus*). Postmortem blood and urine samples were available for analysis. All routine urine and blood toxicology screens were negative. The LC-MS/MS method allowed sensitive quantification of aconitine, the main toxin in *A. napellus*, and showed 3.6 and 149 mug/L in blood and urine, respectively. These concentrations were similar to that reported in other aconitine-related deaths. This case illustrates the dangers of consuming unidentified plants, and documents concentrations of aconitine in blood and urine in a fatal case of *A. napellus*-related poisoning.
30. Ramjan KA, Williams AJ, Isbister GK, Elliott EJ. 'Red as a beet and blind as a bat' Anticholinergic delirium in adolescents: lessons for the paediatrician. *J Paediatr Child Health.* 2007;43(11):779-80. PMID: 17924941
Anticholinergic syndrome has been widely documented in the literature but is uncommon in paediatric medicine. Teenage boys are most at risk of self-induced anticholinergic syndrome through intentional ingestion of plants. We report on a 14 year old boy who presented to our hospital with clinical signs of anticholinergic toxicity and who was discharged 36 hours after admission with no major residual effects. Classical anticholinergic syndrome should be readily diagnosed by the experienced clinician ('hot as a hare, red as a beet, dry as a bone, blind as a bat and mad as a hatter'). Acute presentations should be treated with benzodiazepines and supportive care. Treatment of the delirium with haloperidol may be harmful. Lack of familiarity with anticholinergic syndrome may also delay the diagnosis or result in potentially harmful treatments. A high index of suspicion is often required in the paediatric setting due to infrequent acute hospital presentation.
31. Schmetzmann M, Williamson A, Black D. Stable age pattern supports role of development in unintentional childhood poisoning. *Inj Prev.* 2008;14(1):30-3. PMID: 18245312
OBJECTIVE: To investigate if child development has a role in unintentional poisoning, by describing the pattern of hospitalization due to unintentional poisoning in children aged 0-4 years in New South Wales by single year of age and then assessing the stability of the age-specific pattern found when analyzed by sex, remoteness of residence, and socioeconomic status. DESIGN: Retrospective descriptive study. SETTING: New South Wales hospitals from 1994 to 2005. PARTICIPANTS: Children aged 0-4 years in the New South Wales Department of Health Inpatient Statistics Collection. Main exposure: Hospitalization due to unintentional poisoning. MAIN OUTCOME MEASURES: Hospitalization rates by single year of age and single year of age by three covariates: sex, remoteness of residence, and socioeconomic status. RESULTS: Children aged 1-3 years had the highest rates of hospitalization due to unintentional poisoning, and this pattern persisted over time. The same age-specific pattern was seen for both boys and girls, but rates were significantly higher for boys than girls at age 3 years (RR = 1.46, 95% CI 1.31 to 1.62). The age-specific pattern persisted when the covariates remoteness of residence and socioeconomic status were controlled for. CONCLUSION: The age-specific pattern of hospitalization for unintentional poisoning by single year of age was found to be stable when analyzed over time and by sex,

remoteness of residence, and socioeconomic status. This finding provides strong evidence for the role of a child's development in an unintentional poisoning event.

32. Settimi L, Davanzo F, Carbone P, Sesana F, Locatelli C, Farina ML, Maiozzi P, Roazzi P, Maccari F, et al. Surveillance of toxic exposures: the pilot experience of the Poison Control Centers of Milan, Pavia and Bergamo in 2006. *Ann Ist Super Sanita*. 2007;43(3):287-94. PMID: 17938460
Between 1 February and 31 March 2006, the Poison Control Centers (PPC) active in Lombardy collaborated with an integrated surveillance system carried out in Piedmont during the Olympic Games 2006. The collaborating PPC notified to the system 697 human cases of exposure occurred in Piedmont during the observation period. Among these cases, 70% were exposed accidentally, 40% were 6 years old or younger, and 45% reported at least a clinical effect. The agents more frequently reported were: cleaning substances (household) (110 cases), fumes/gases/vapors (63 cases, comprising 38 cases accidentally exposed to carbon monoxide), and sedative/hypnotics/antipsychotics (53 cases). Although very limited, the available observations focused the attention on specific hazards and were able to highlight the potential of a toxic exposure surveillance system based on the information reported by the Italian PPC.
33. Skalli S, Zaid A, Soulaymani R. Drug interactions with herbal medicines. *Ther Drug Monit*. 2007;29(6):679-86. PMID: 18043467
The use of herbal medicines (HM) is on the rise among the global population. Although the safety profile of many herbal medicines is promising, accumulated data show evidence of significant interactions with medications, which can place individual patients at great risk. A range of electronic databases have been reviewed for articles published in this field: Medline, Allied and Complementary Medicine Database, HealthSTAR, AMBASE, CINHALL, Cochrane Library, as well as Internet documents and manually searched references in medical journals. In this review, we examined the literature from 1966 to 2006 and focused on the importance of the risk of drug interactions and potential side effects when HM are involved. We discuss these in light of the documented findings. A review of the problematic issues is given and recommendations are made in order to encourage the setting up of clinical trials on HM and herb-drug interactions.
34. Stummann TC, Hareng L, Bremer S. Embryotoxicity hazard assessment of methylmercury and chromium using embryonic stem cells. *Toxicology*. 2007;242(1-3):130-43. PMID: 17980949
The embryonic stem cell test (EST) has been scientifically validated (2001) as an in vitro embryotoxicity test, showing a good overall test accuracy of 78%. Methylmercury (MeHg) was the most significant outlier identified, as the metal was the only strong in vivo embryotoxicant falsely predicted to be non-embryotoxic. The EST misclassification of MeHg, and the potential environmental exposure and developmental toxic hazards of heavy metals gave us the rationale to investigate whether the EST can correctly predict the embryotoxic potential of two heavy metals different from MeHg. The EST correctly classified trivalent chromium to be non-embryotoxic and hexavalent chromium to be embryotoxic, while we confirmed the misclassification of MeHg. MeHg causes developmental abnormalities in the brain. We therefore aimed to improve the in vitro prediction of MeHg embryotoxicity by including a neuronal ES cell differentiation assay. Differentiation of neuronal-like cells was demonstrated by real-time PCR experiments, showing up-regulation of several neuronal marker genes, and immunohistochemistry, demonstrating the appearance of nestin, neurofilament medium polypeptide, beta-tubulin III and microtubule-associated protein 2 (Mtap2) positive cells. We identified Mtap2 mRNA expression as a sensitive toxicological endpoint for MeHg-induced neuronal embryotoxicity, as Mtap2 mRNA was down-regulated in the presence of non-cytotoxic concentrations of MeHg. Noticeably, several other neuronal marker genes were unaffected by MeHg and Mtap2 expression was not affected until day 14 of differentiation. This implies that the total neuronal-like cell number was unchanged and that the down-regulation of Mtap2 expression reflects neuron-specific toxicity, i.e. instability of the neuron-specific microtubules, and arrest of the neuronal maturation. The fact, that most marker

genes were unaffected by MeHg, stresses the importance of including an array of marker genes. In conclusion, our results imply that inclusion of additional target tissues and refinement of the current prediction model may enhance the predictive power of the EST.

35. Subrahmanyam D, Mathew J, Raj M. An unusual manifestation of Abrus precatorius poisoning: A report of two cases. *Clin Toxicol (Phila)*. 2008;46(2):173-5. PMID: 18259968
Abrus precatorius seeds are highly toxic and are often ingested as a means of suicide in India. Hemorrhagic gastroenteritis with erosions, hemolysis, acute renal damage, hepatotoxicity with elevated liver enzymes, and seizures are common manifestations of toxicity. We report two cases of Abrus precatorius poisoning with raised intracranial pressure (ICP) and papilledema that have not been described earlier in literature. One patient recovered completely with conservative management to lower raised ICP while the other patient expired before effective treatment could be instituted. The cases are being reported to propose the need for routine fundus examination and brain imaging in severe abrus poisoning with CNS toxicity, as early institution of treatment for cerebral edema measures may be life saving.