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ABSTRACTS

Abstracts of the 2010 International Congress of the European Association of Poisons Centres and Clinical Toxicologists, 11-14 May 2010, Bordeaux, France

1. Investigation of the Poisoned Patient - History Taking and Physical Examination

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Background: Assessment of an acutely poisoned patient involves the taking of an appropriate history, assessment of the vital signs, level of consciousness, a physical examination, and requesting appropriate toxicological and non-toxicological investigations. Diagnosis is based on the history, circumstantial evidence, a cluster of symptoms and signs, on the results of biochemical and toxicological analyses and ECG or X-ray abnormalities. Poisoning should be suspected in all cases of sudden, severe, and unexpected illness and in any patient who presents with multisystemic involvement. *History:* In many cases, it is not difficult to make the correct diagnosis because a history of drug overdose or exposure to the toxic agent is provided by the patient, family members, witnesses or emergency services staff. If the patient is unable to provide accurate information (very young, unconscious, demented) circumstantial evidence may be important in establishing the diagnosis. In previously healthy young adults, self-poisoning is probably the reason for unexpected coma. When unconscious patients are found with empty drug packages, alcoholic beverages, household product containers, it is reasonable to suspect that these agents may be the cause of coma. Suicide notes, sent SMS or e-mails will support the assumption of self-poisoning. The surrounding circumstances and the place of discovery may suggest poisoning with a specific agent (e.g. carbon monoxide poisoning in the bathroom with gas water heater or in the garage). In an unsupervised child, circumstances often suggest that the substance in the mouth or on the skin has been swallowed. The patient's medical or psychiatric history, current medications used by patient or family members, obtained from family or friends if the patient is unable to relate the information, may imply a likely cause of poisoning. *Physical examination:* Findings on physical examination are of great clinical value. The general appearance of the patient, including vital signs, skin color and lesions, skin and breath odor, may give important diagnostic features. The patient who has taken an overdose often exhibits varying clinical signs, with alteration in cardiovascular (e.g. hypotension, hypertension, dysrrhythmias), respiratory (e.g. reduced respiratory rate and airway reflexes), and neurological (loss of consciousness, convulsions, corneal and pupillary reflexes, and spinal reflexes) functions. Other signs, e.g. needle tracks, pressure marks, bullous lesions and soft tissue swelling, may also be present. Several clinical patterns may also be typical for different types of poisoning and these can be a useful guide to discovering the agent responsible, laboratory tests needed and treatment required. The presence of toxidromes "clusters of symptoms and signs in the same patient" will be of considerable diagnostic value. Toxidromes due to opioids, anticholinergics, cholinergics, sympathomimetics and salicylates are the most readily recognizable. *Conclusion:* Careful history taking and physical examination allow the establishment that a patient's symptoms and signs are the result of exposure to one or more chemical substances.

2. The Principles of Blood Tests in Adult Toxicology

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Objective: To explain the purpose and value of blood tests in adult toxicology. *Method:* The possible reasons for undertaking blood tests are considered with regard to diagnosis and management of poisoning in adults. *Results and discussion:* Blood tests should only be done with a clear purpose in mind, and once requested, the results should be found and acted upon. Some simple biochemical tests can be helpful in making a diagnosis of poisoning and guiding treatment, and it is reasonable to check them in all patients where poisoning is possible: urea, creatinine, sodium, potassium, chloride, (venous) bicarbonate, glucose. Abnormal results in these measurements can suggest what further testing will be appropriate. Functional tests, such as prothrombin time in patients who have taken coumarins, may be essential to the satisfactory management of some overdoses. Some toxicological tests need to be carried out as they may give the only clue to diagnosis. Testing for paracetamol (acetaminophen) is the most frequent example of a test whose omission in the investigation of an unconscious or uncommunicative patient, can be disastrous. Other toxicological tests will be needed to diagnose toxic causes for clinical syndromes, which may be anything from sudden unconsciousness to chronic peripheral neuropathy. The diagnostic tests can be tailored to the clinical syndrome. The diagnosis of the cause of death is a particular challenge, and results can be seriously misleading. Drugs with narrow therapeutic ranges, e.g. lithium and digoxin, are good examples of poisons where measurement of serum concentration can be very helpful in management. Others include iron (with total iron binding capacity), ethylene glycol and methanol; and antiepileptic agents in patients with epilepsy. Sensible tests: urea, electrolytes, and creatinine; venous bicarbonate; glucose, ANION GAP = [cSODIUM + cPOTASSIUM] - [cBICARBONATE + cCHLORIDE] Essential tests, where knowing the concentration may be the only clue: paracetamol (acetaminophen)Tests suggested by clinical circumstances: drug concentrations, where the result might alter management - lithium, salicylate, iron, methanol, ethylene glycol. Tests where knowing the concentration usually does not alter management: opioids (give naloxone); tricyclics (give support); benzodiazepines (give support, flumazenil). Drug screening may be helpful for several clinical syndromes: alopecia; cardiac arrhythmia or infarction in younger patients; respiratory arrest; aggression; confusion; peripheral neuropathy; unconsciousness; unexpected death. Functional tests can be useful, e.g. prothrombin time in patients who have taken coumarins; cholinesterases in patients who have taken organophosphorus compounds. *Conclusion:* careful choice of tests can substantially improve the diagnosis and management of poisoning, and the cost-effective utilization of the laboratory.

3. Investigation of the Poisoned Patient: Place of Cardiovascular Monitoring

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Objective: Drug-induced hypotension is a common feature in acute poisonings, related to various mechanisms.[1] Circulatory failure represents a life-threatening complication requiring close monitoring of the patient's hemodynamic conditions in intensive care (ICU). Despite significant improvement in critical care, drug-induced cardiovascular failure remains a leading cause of death.[2] Cardio-toxicants include not only the cardiovascular drugs but also various other toxicants like antidepressants, H1-antihistaminic agents, meprobamate, chloroquine, cocaine, organophosphates, cyanide, and plants.[3] The objective is to discuss the role and indications for the different available tools and techniques for cardiovascular monitoring in acute poisoning. *Methods:* Review of PubMed-referenced studies. *Results:* Physiology rules teach us that vascular perfusion pressure is determined by three factors: the stroke volume, the heart rate, and the systemic vascular resistance. Any alteration in one of these factors immediately results in a compensation by the two others, unless some degree of drug-induced failure of these mechanisms occurs leading to hypotension. Shock is defined as 1) systolic blood pressure <90 mmHg or decrease in usual systolic blood pressure >40 mmHg or mean blood pressure <65 mmHg, 2) unresponsive to fluids, 3) with at least one sign of organ hypoperfusion. While blood pressure and heart rate only describes "macrocirculation", circulatory failure results from the inability of circulation to meet the metabolic cell demand, expressed as impairment of "microcirculation". Alteration in microcirculation is usually evidenced by the occurrence of symptoms or signs including dizziness, loss of consciousness, collapse, chest pain, or skin discoloration. Consequently, repeated assessment of changes in mental status and urine output as well as chemical tests including plasma lactate, serum creatinine, and liver enzymes, is mandatory to guide adequate treatments. Determination of hypotension mechanism is mandatory to improve patient management. Providing preload parameters is useful to optimize fluids. Measurement of cardiac index is essential to distinguish between cardiogenic (<2.5 L/min/m^2) and peripheral failure (>3.5 L/min/m^2). Heart failure mainly results from decreased systolic myocardial contractility.[3] However, other mechanisms may also be implicated, including diastolic dysfunction, alteration in heart contraction geometry, myocarditis or acute coronary syndrome. For instance, overdoses with calcium-channel blockers, beta-blockers, and membrane-stabilizing agents may result in myocardial negative inotropic effects as well as arterial dilatation. Besides invasive blood pressure (using an arterial catheter) and electrocardiogram monitoring, circulation conditions can be assessed using a large number of bedside devices. Echocardiography coupled with Doppler allows a direct visualization of the heart contractility and aspects (ventricle dilatation, myocardium thickness, valve diseases); however, it remains operator-dependent.[4] Right heart catheterization, traditionally performed by all intensivists, allows the thermodilution-based measurement of cardiac output as well as the simultaneous determination of arterial and mixed venous blood gases providing insights on

oxygen transfer, delivery and consumption; however, it is invasive with potential complications and the exact significance of the mean pulmonary artery wedge pressure remains debated.[5] Oesophageal Doppler technique (4 MHz continuous or 5 MHz pulsed wave Doppler transducer) is based on the measurement of blood flow velocity in the descending aorta at the tip of a flexible probe.[6] Accurate velocity measurement requires good alignment between the Doppler beam and blood flow. Achieving adequate probe positioning to obtain reproducible cardiac output requires a significant learning curve with the technique. Minimally invasive techniques with easy-to-use platforms providing adequate evaluation and monitoring of cardiac output are now widespread in ICUs, based on transpulmonary peripheral arterial thermodilution and pulse contour analysis (PiCCOTM system, Pulsion Medical Systems, Munich, Germany),[7] lithium dilution and pulse power analysis (LiDCO™plus, LiDCO Ltd, Cambridge, UK),[8] and pulse contour analysis (Vigileo-FloTrac™ system, Edwards Lifesciences, Irvine, CA).[9] Additionally, PiCCOTM system allows the measurement of extravascular lung water that may be interesting to distinguish between both causes of pulmonary oedema (cardiac failure versus pulmonary injury). These systems are particularly interesting for rapid insight into the unstable poisoned patient's hemodynamic conditions, allowing rapid decisions regarding the requirement of extracorporeal life support. However, due to the absence of validation of the arterial pressure waveform-based methods in all conditions (e.g. spontaneous breathing, cardiac arrhythmia), further investigation is still required with regard to their ability to guide goal-directed therapy. Recently, more sophisticated devices allow the poor invasive assessment and monitoring during resuscitation of microcirculation including continuous SVO_2 measurement, sublingual capnometry (carbon dioxide pressure monitoring using a microelectrode sensor, Capnoprobe SL Model 2000 Sensor, Optical Sensor Inc., MN, USA), and Near Infrared Spectroscopy-based tissue oxygenation (InSpectraTM StO_2 monitor). *Conclusions:* Drug-induced circulatory failure is common and life-threatening in acute poisonings. Several "old" and "recent" devices exist to monitor the patient's circulation, either in its "macro-component" (blood pressure and cardiac output) or its "micro-component" (tissue dysfunction). Early determination of the mechanism of drug-induced circulatory failure as well as the continuous monitoring of hemodynamic conditions is helpful to improve poisoning management in the ICU. *References:* 1. Albertson TE, Dawson A, de Latorre F, et al. TOX-ACLS: toxicologic-oriented advanced cardiac life support. Ann Emerg Med 2001; 37:S78–90. 2. Bronstein AC, Spyker DA, Cantilena LR Jr, et al. Clin Toxicol (Phila) 2008; 46:927–1057. 3. Mégarbane B, Aslani AA, Deye N, et al. Pharmacokinetic/pharmacodynamic modeling of cardiac toxicity in human acute overdoses: utility and limitations. Expert Opin Drug Metab Toxicol 2008; 4:569–79. 4. Salem R, Vallee F, Rusca M, et al. Hemodynamic monitoring by echocardiography in the ICU: the role of the new echo techniques. Curr Opin Crit Care 2008; 14:561–8. 5. Richard C, Warszawski J, Anguel N, et al. Early use of the pulmonary artery catheter and outcomes in patients with shock and acute respiratory distress syndrome: a randomized controlled trial. JAMA 2003; 290:2713–20. 6. Singer M. Oesophageal Doppler. Curr Opin Crit Care 2009; 15:244–8. 7. Mayer J, Suttner S. Cardiac output derived from arterial pressure waveform. Curr Opin Anaesthesiol 2009; 22:804–8. 8. Pearse R, Ikram K, Barry J. Equipment review: an appraisal of the LiDCO plus method of measuring cardiac output. Crit Care 2004; 8:190–5. 9. Compton FD, Zukunft B, Hoffmann C, et al. Performance of a minimally invasive uncalibrated cardiac output monitoring system (Flotrac/Vigileo) in haemodynamically unstable patients. Br J Anaesth 2008; 100:451–6.

4. Inhalational Exposure to Chemical agents Causing Acute Lung Injury

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Introduction: Physicians should be prepared for inhalational exposure to chemical agents to be able to organize adequate medical aid in cases of unexpected releases and terrorist attacks. Depending on the agent involved, they can be dispersed as gas/vapor or aerosol (mists, fumes, smokes, or dusts). Increased humidity increases particle size by hygroscopic effect. Particle distribution depends on particle size, speed and depth of inhalation. *Clinical aspects:* Symptoms depend on substance concentration and toxicity, exposure duration, water solubility, respiratory minute ventilation, and individual susceptibility. Gases that are highly soluble in water affect upper airways more than peripheral airways. Instantly after exposure clinical symptoms appear and may consist of nasal discharge, lacrimation, dyspnea, bronchospasm, bronchial edema, and cyanosis. After exposure to less water soluble gases more peripheral airway and alveoli effects can be expected. In the first hours, symptoms can be absent. Thereafter, depending on concentration and exposure duration, acute lung injury can become manifest. *Conclusion:* It is pivotal to know substance and type of clinical symptoms involved. Supportive therapy is essential (e.g. oxygen supply, bronchodilating medicines, mechanical ventilation). There is no evidence that corticosteroids, radical scavengers or prophylactic administration of antibiotics diminish the clinical effects or survival.

5. Correlation Between Arterial and Venous Lactates and Blood Gases in Acute Poisonings Treated with Extracorporeal Life Support for Refractory Cardiac Failure or Arrest

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Objectives: Extracorporeal life support (ECLS) has been proposed as an alternative rescue method to treat patients suffering from cardiac failure or arrest if not responding to conventional treatment and cardiopulmonary resuscitation. Our aims were: 1) to study the correlations between arterial and venous lactates and blood gases in these poisonings associated with extremely poor cardiovascular conditions and 2) to assess their respective predictive values regarding survival at 24h in case of cardiac arrest and ICU discharge in case of cardiac failure. *Methods:* We designed a prospective study including all ECLS-treated patients in our toxicological ICU with arterial and venous samplings obtained at the time of femoral vessel cannulation to measure lactates and blood gases. We calculated the inotropic score, roughly representing the severity of myocardial dysfunction (IS (µg/kg/min) = dopamine + dobutamine + isoprenalinex100 + adrenalinex100 + noradrenalinex100). Results were expressed as median [25–75%-percentiles]. Correlations were performed using Pearson tests, univariate comparisons using Chi-2 and Mann-Whitney tests, and multivariate analysis using logistic regression with Odds ratio (OR) and 95%-confidence interval determination. *Results:* Twenty-eight patients (10M/18F, 42 years [34–51], SAPSII: 82 [72–89]) were included. Among these patients, 16 were in refractory cardiac arrest (low flow: 150 min [105–172], 24h-survival rate: 47% and ICU survival rate: 11%), while 12 were in severe cardiac failure (inotropic score: 145 µg/kg/min [105–243] and ICU survival rate: 67%). Poisonings involved sodium-channel blockers (21/28), meprobamate (2/28), and calcium-channel blockers (1/28). Whatever the indication for ECLS was, correlations between arterial and venous lactate (R^2 = 0,78), bicarbonate (R^2=0.85), base excess (R^2=0.92), pH (R^2=0.88), and PCO_2 (R^2=0.49) were good (p<0.0001). In contrast to the low-flow duration, none of these parameters was significantly associated with the 24h-survival rate in cardiac arrest patients. Based on a multivariate analysis, the arterial lactate concentration measured at the time of cannulation (9.4 mmol/l [6.3–12.2]) was the only predictive factor of survival in ECLS-treated patients for cardiac failure (OR: 16 [1.1–234.3] for lactate concentrations >8 mmol/L). *Conclusion:* Despite good correlations between their corresponding parameters, arterial and venous samplings remain complementary in case of extremely poor cardiac conditions to better evaluate oxygenation level as well as the respiratory/metabolic acidosis proportions.

6. A Systematic Review of the Use Of Intravenous Lipid Therapy in the Management of Poisoned Patients

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Introduction: Intravenous lipid therapy (ILE) in the context of this summary refers to the parenteral administration of a lipid-containing emulsion in an attempt to ameliorate the adverse effects of drug or chemical toxicity. The rationale for ILE derives from data generated four decades ago which suggested a pharmacokinetic interaction between lipophilic medications and an administered lipid emulsion.[1,2] The potential therapeutic utility of a lipid-chemical interaction was first reported in 1998, by Guy Weinberg, an anesthesiologist from the University of Illinois, in a rat model of bupivacaine-induced cardiac arrest.[3] In the Weinberg model rats were attempted to be resuscitated from cardiac arrest with either saline or ILE, the latter by the administration of a 30% lipid emulsion. Intravenous lipid therapy was associated with an approximately 50% increase in the LD50 for bupivacaine. *Discussion:* Nineteen additional animal studies have been identified by the author as fully published in the English language literature, eleven of which were published in 2008–9. These studies are comprised of 7 on bupivacaine, 4 on beta-receptor antagonists, 3 on cyclic antidepressants, 3 on verapamil and 1 each on thiopentone, paraoxon, and asphyxia. A number of different animal species have been used in these studies: rats in 10, canines in 2, pigs in 2, rabbits in 5, and one in the mouse. Sixteen of these twenty controlled experimental studies showed often very dramatic beneficial effects of ILE, including those with the end point of resuscitation from full cardiac arrest. Other endpoints in which therapeutic efficacy has been demonstrated are coronary perfusion pressure, blood pressure, heart rate and QRS duration. In comparative studies ILE was superior to saline, vasopressin, epinephrine, and in the case of verapamil, to atropine and calcium. In contrast, in asphyxial cardiac arrest ILE was not superior to standard Advanced Cardiac Life Support.[4] Human experience with ILE is mostly anecdotal and has not been the subject of a controlled study in poisoned patients. However, coincident with the proliferation of controlled experimental studies on animal models in the last two years there has been a growing number of anecdotal reports in humans. To date the author has identified 15 published English-language case reports, 11 of which were published in 2008 and 2009. These have documented successful, and at times remarkably impressive, resuscitations including several cases of apparent dramatic reversal of prolonged cardiac arrest with a lack of subsequent neurological deficits. Nine of the human case reports have involved local anesthetics, 7 with bupivacaine alone, 1 with a combination of mepivacaine and bupivacaine, and 1 with ropivacaine. The other cases have involved one each of an overdose of bupropion, sertraline and Seroquel, verapamil, verapamil and atenolol, atenolol alone, and haloperidol. There has also been a case report of a dog with moxidectin toxicity successfully treated by ILE. To date there have been no major adverse effects of ILE reported. However, ILE appears to be less effective in animal models when high doses of epinephrine are administered.[5,6] *Conclusions:* Based on a critical analysis of this literature it may be concluded that there is clear and unambiguous evidence of the efficacy of ILE in animal models. In contrast, "real world" experience with poisoned humans is completely anecdotal and, undoubtedly, suffers from the publication bias

inevitably associated with the very low likelihood that the non-resuscitated patient would be published. Power considerations suggest that it is unlikely that there will be a prospective controlled clinical trial of ILE in humans with major manifestations of drug toxicity. However, prospective accumulation on experience with ILE has now been undertaken by several ongoing studies. Currently the Association of Anaesthetists of Great Britain and Ireland and the Resuscitation Council of the UK have established guidelines for the use of ILE in local anesthetic toxicity. These are available on their websites. *References:* 1. Krieglstein J, Meffert A, Neimeyer D. Influence of emulsified fat on chlorpromazine availability in rabbit blood. Experientia 1974; 30:924–6. 2. Shah A, Sawchuk R. Effect of co-administration of Intralipid on the pharmacokinetics of cyclosporine in the rabbit. Biopharm Drug Dispos 1991; 12:457–66. 3. Weinberg G, VadeBoncouer T, Ramaraju G, et al. Pretreatment or resuscitation with a lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats. Anaesthesiol 1998; 88:1071–5. 4. Harvey M, Cave G, Kazemi A: Intralipid infusion diminishes return of spontaneous circulation after hypoxic cardiac arrest in rabbits. Anesth Analg 2009; 108:1163–8. 5. Weinberg GL, DiGregorio G, Ripper R, et al. Resuscitation with lipid versus epinephrine in a rat model of bupivacaine overdose. Anesthesiol 2008; 108:907–13. 6. Hiller DB, DiGregorio G, Ripper R, et al. Epinephrine impairs lipid resuscitation from bupivacaine overdose. Anesthesiol 2009; 111:498–505.

7. Incidence of Adverse Cardiovascular Events Following Drug Overdose: A Pilot Study

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Objective: Drug overdose is a leading cause of cardiac arrest in victims under 45 years of age, and is the second leading cause of injury related fatality in the US. Risk factors for adverse cardiovascular events (ACVE) in emergency department (ED) patients with acute overdose have previously been derived, but the incidence of ACVE following hospitalization for acute drug overdose is unknown. This pilot study characterizes the incidence of in-hospital ACVE following acute drug overdose in patients presenting to the ED. *Methods:* This pilot, prospective cohort study enrolled consecutive adult ED patients with acute drug (medication and illicit) overdose in one urban, tertiary care hospital over 12 months (2007–08). Subjects were prospectively followed to hospital discharge with data that included electronic medical records, ED paper records and inpatient telemetry monitoring (if any). In-hospital ACVE were defined as the occurrence of ≥1 of the following: myocardial injury (troponin > 0.09 ng/mL), shock (hypotension requiring vasopressors), ventricular dysrhythmia (VT, VF, or TdP), and cardiac arrest (loss of pulses requiring CPR). Descriptive statistics and 95% confidence intervals were calculated. *Results:* There were 459 eligible ED patients with suspected drug overdose. One hundred and eighty-six patients were excluded (61 chronic toxicity, 50 children aged <18, 49 non-drug overdose, 13 alternate diagnosis, 6 dermal/inhalational exposure, 5 insufficient data, 1 anaphylaxis), leaving 273 subjects included for analysis (mean age 40.3, 63% male, 1.8% mortality). During the study period, the following numbers of ACVE were recorded: 12 (4%) myocardial injury, 3 (1%) shock, 2 (1%) dysrhythmia, and 3 (1%) cardiac arrest. The overall incidence of ACVE was 5.9% (95% CI 3.1–8.6%). In 16 patients with ACVE, 75% were multi-drug overdoses with the most frequent exposures being opioids (7 total, 4 methadone), benzodiazepines (7), and cocaine (5). *Conclusion:* Based on this pilot study, ACVE may occur in up to 8.6% of adult patients with acute drug overdose. Implications for the evaluation and triage of ED patients with acute drug overdose require further study with regard to optimization of adverse event prediction.

8. What is the Evidence for Added Benefit from Hemoperfusion? Pro

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Objective: To review the potential benefits and the evidence for charcoal hemoperfusion (CHP) in the treatment of intoxicated patients. *Methods:* Review of the international literature. *General considerations:* The optimal method of extracorporeal elimination of xenobiotics is often a matter of debate. Due to the lack of well-designed clinical trials we are left with circumstantial evidence as to whether extracorporeal drug removal is beneficial and if so, by what method. However, most clinicians would agree that in the case of ongoing toxicity in a life-threatening poisoning, the faster one removes a toxin, the less chance of toxicity. Beside hemodialysis (HD), CHP provides a potential tool for enhanced drug elimination. *Results:* During recent years, there was an increase in reported use of HD and a decrease in the use of CHP in poisoning emergencies. The former is mostly linked to an increase in overdoses with lithium and toxic alcohols, the latter to the infrequency of intoxications with theophylline and phenytoin, both classical candidates for CHP[1]. Like HD, CHP is most effective for toxins that have a small volume of distribution. Unlike HD, it also can effectively remove toxins that are bound to plasma proteins or with a higher molecular weight. Commonly cited side effects of CHP like thrombocytopenia and hypocalcemia are less frequent since the introduction of biocompatible membranes and are often self-limiting. Generally accepted drugs amenable to elimination by CHP are barbiturates (I), carbamazepine (II), theophylline (III) and phenytoin (IV). Furthermore, valproate (V), paraquat (VI) and amatoxins (VII) are also toxins that could be effectively removed by CHP. (I) Long acting barbiturates (Vd=0.5 L/kg; Pb=0.5): As barbiturates bind readily to AC, they are promising to be effectively eliminated by CHP. Half-life during HP is about 3.2 hrs compared to 27 hrs during HD and the elimination rate is about ten-fold compared to HD.[2] There are a number of case reports and series which describe dramatic improvements of clinical condition (e.g. time to wake up, time to extubation, length of stay). However, its effectiveness regarding improvement of outcome is not yet proven. (II) Carbamazepine (Vd=0.8–1.8 L/kg; Pb=0.75): CHP seems to be equivalent to high-flux dialysis. CHP may reduce serum concentration up to 50% and shorten half-life (6 hrs versus 2–6 days). During CHP, an improvement of cardiovascular stability and a decrease in coma time, mandatory ventilation and need for vasopressor support is frequently cited.[3] (III) Theophylline (Vd=0.45 L/kg; Pb=0.4–0.65): It binds readily to AC and CHP can enable 4–6 fold clearance rates and extraction ratios up to 0.75 compared to native elimination. Again, CHP reduces duration of clinical intoxication, decreases heart rate, increases blood pressure and reduces serious CNS-side effects. In a prospective, 10-year observational study (n=56), fewer patients treated with CHP developed major toxicity (18% vs. 33%) and exhibited higher drug clearance rates (295 vs. 185 mL/kg/hr) compared to HD.[4] (IV) Phenytoin (Vd=0.6–0.8 L/kg; Pb=0.8–0.9): It shows a greatly increased half-life in overdose that can be decreased from 86 hrs to 10 hrs by performing CHP, along with impressive improvements in consciousness. Urgent lowering of phenytoin in plasma is associated with a reduced risk of irreversible cerebellar atrophy, favouring CHP as the elimination of choice.[5] (V) Valproate (Vd=0.1–0.4 L/kg; Pb=0.9–0.95): Valproate is eliminated up to 10 fold by CHP or high-flux HD compared to its native clearance suggesting the combination of HD and CHP as the most effective treatment. Extraction rates up to 0.41 could be achieved together with clinical improvements regarding length of coma and the need for ventilatory or circulatory support.[6] (VI) Paraquat (Vd=1.2–1.6 L/kg, Pb<0.06): Its low endogenous clearance (24 mL/min/kg) is further diminished in overdoses with renal insufficiency at plasma paraquat-level >1 mg/L. In a series of 23 overdoses, mortality rate in the CHP group was 67% compared to 75% in the supportive care only group. In another review of 42 paraquat overdoses, improvement in the length of survival could only be achieved if CHP was performed in the first hours after ingestion with paraquat in plasma <3 mg/L, but it did not improve overall outcome.[7] Due to its extensive tissue binding, a re-increase of paraquat in plasma is often observed after termination of CHP and the amount that could be eliminated by CHP is often negligible. (VII) Amatoxins (Vd=0.5–0.9 L/kg; Pb=negligible): They are detectable in plasma up to 24–48 hrs p.i., suggesting CHP as a reasonable elimination technique. It is assumed that lowering the available amount of amatoxins might decrease cell injury thus limiting its hepatotoxic potential. Additionally, amatoxins are well bound to AC or resin. A number of case series demonstrated survival rates from 65–100% with the use of CHP. *Conclusion:* CHP remains an important, but secondary method of treatment in individual, life threatening overdoses. In every case, suitable pharmacokinetics of the poison is mandatory for being effectively eliminated. CHP can never be substituted for excellent supportive care or specific antidotal treatment. It is unlikely that we will be faced with a controlled study in the future to definitely evaluate the effectiveness of CHP in an evidence-based fashion. *References:* 1. Holubek W, Hoffman R, Goldfarb D, et al. 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9. Diethylene Glycol Poisoning: from Metabolism to Treatment

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Background: Consumer exposure to diethylene glycol (DEG) is widespread because it is commonly used in commercial solvents and automotive products. DEG has recently gained international notoriety because of numerous highly-fatal poisoning epidemics of renal failure that resulted from its mistaken substitution as a solvent in medications. Despite vast publicity about these mass poisonings, there is virtually nothing known about the mechanism of its toxicity. More importantly, hemodialysis seems to be the only defined, effective treatment available today. Human DEG poisonings typically show a metabolic acidosis, acute renal failure, mild hepatotoxicity, neurologic impairment (facial nerve paralysis) and death, particularly with inadequate treatment. Autopsy of human cases has shown severe renal cortical necrosis, with a milder hepatic pathology. Studies in animals including rats, rabbits and dogs have shown a similar toxicity, with acute renal failure being the predominant feature. At low doses of DEG in animals, unchanged DEG is the major product in the urine, with 2-hydroxyethoxyacetic acid (HEAA)

being the primary metabolite. In addition, in human case studies involving nearly 100 individuals, no oxalate has been detected in the urine, nor have kidney sections contained oxalate crystals. As such, DEG is primarily metabolized by alcohol dehydrogenase (ADH) to hydroxethoxyacetaldehyde, which is then rapidly converted to HEAA. HEAA could be further oxidized to diglycolate (DGA), although this has not been shown *in vivo*. A few clinical studies have suggested that DEG itself may be toxic (because of neurologic sequelae), but the prevailing view is that DEG produces toxicity because of its metabolism. However, no studies have related the appearance of HEAA or any other metabolite in the blood or target tissue with the resulting toxicity in tissues. Ongoing studies in animals have been designed to examine the metabolism and mechanism of toxicity of DEG in order to aid in the development of improved clinical treatments. *Methods:* Male rats were placed in one of four treatment groups including: water, low dose DEG (2 g/kg), high dose DEG (10 g/kg), or high dose DEG + fomepizole (to inhibit ADH). Blood and urine samples were collected up to 48 h to assess development of toxicity and metabolite accumulation. *Results:* Rats treated with high dose DEG developed metabolic acidosis, moderate to severe renal toxicity and mild liver damage. No signs of any toxicity were observed in the DEG + fomepizole-treated group throughout the time course. Histopathologic studies on kidneys revealed that DEG induced a proximal tubular necrosis that was also blocked by treatment with fomepizole. Metabolic studies confirmed that urinary excretion of unchanged DEG accounted for >50% of the DEG doses (about 95% of the dose when given with fomepizole). Urinary excretion of HEAA and DGA represented 25–35% and 1% of the dose, respectively. Fomepizole completely blocked DEG metabolism since no HEAA or DGA was excreted in the urine of these rats. Urinary HEAA excretion correlated with the metabolic acidosis and was associated with the degree of renal toxicity. These results demonstrate that HEAA was the major acidic metabolite in urine after toxic doses of DEG and suggest that HEAA may be responsible for the target organ toxicity of DEG. However, when normal human proximal tubule cells were treated with DEG (up to 100 mM), HEAA or DGA (both at up to 25 mM) for 6 h, cell death was not observed. Instead, toxicity to these cells did increase with a 48 h exposure to both HEAA and DGA in a dose dependent manner. *Conclusion:* These results demonstrate for the first time that a metabolite(s) of DEG, rather than DEG itself, is responsible for its toxicity and that fomepizole may be useful for treating DEG poisoning by blocking its metabolism. HEAA appears to be the toxic metabolite of DEG, but determination of the plasma and kidney tissue metabolite levels are needed to confirm that its accumulation relates to the development of DEG toxicity. Interestingly, toxicity of DEG metabolites on human kidney cells in culture is observed only with prolonged exposure. Studies on the mechanism by which HEAA produces toxicity will be useful for designing alternative treatments in cases where metabolic inhibition is not possible.

10. The Relative Toxicities of Glycols

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Objective: Diethylene glycol (DEG), and other glycol ethers (OGE) are in numerous products responsible for exposures reported to poison centers. "Glycol" is often a source of considerable confusion as manufacturers' labels often do not specify which glycol is in a formulation. As a result lay persons and medical personnel often wonder if these products are as dangerous as ethylene glycol (EG). This was an observational study comparing the relative risk (RR) of a serious outcome for each type of glycol exposure. *Methods:* We reviewed 1947 exposures to DEG, OGE, and EG reported to a statewide poison control network from 2000 to 2007. Inclusion criteria were patients with any type of oral exposure and a known outcome without coexposure. The percentage of patients who received 4MP, hemodialysis (HD), or with acidosis was determined. *Results:* See Table 1. DEG was found to be associated with a much lower incidence of major adverse outcomes compared to EG (RR of 0.33). OGE exposures from cleaning products may cause significant morbidity, however this study shows that it is quite rare with a RR of 0.08 compared to EG. Intentional ingestions in adults or accidental ingestions in children less than two years were associated with a worse outcome for DEG and EG. *Conclusion:* While DEG and OGE have the potential for serious toxicity exposures to these agents are significantly less dangerous than exposures to ethylene glycol. Future guidelines for glycol exposures may take this into consideration.

11. Extracorporeal Removal Techniques for Toxic Alcohol Poisoning: Indications and Management

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Objectives: Ethylene glycol (EG) and methanol are responsible for accidental, suicidal, and epidemic poisonings, resulting in death or permanent sequelae. Toxicity is due to the metabolic products of alcohol dehydrogenase (ADH) and aldehyde dehydrogenase. Poisoning management is based on the blockade of EG and methanol ADH-mediated metabolism using ethanol or fomepizole, the more recently recommended first-line antidote, while no comparative study of efficacy exists. Our objectives were to determine the current place of extracorporeal removal techniques in toxic alcohol management, taking into consideration the prescribed antidote. *Methods:* Review of PubMed-referenced studies. *Results:* If administered early, both antidotes are efficient in preventing renal injury in EG poisoning and ocular toxicity in methanol poisoning. In the absence of renal failure, EG clearance is rapid, avoiding the need for prolonged antidote administration. In contrast, the long elimination half-life of methanol (about 52h under fomepizole) with absent hemodialysis, necessitates a prolonged antidote course: this is possible with fomepizole but not conceivable with ethanol. Studies showed that up to 85% patients had ethanol concentrations above the therapeutic limit (>1 g/L). While dialysis is often mandatory, adjustment of maintenance ethanol infusion rate represents an additional difficulty to avoid central nervous system side-effects. Hemodialysis is considered to be an integral part of the treatment of toxic alcohol poisonings to expedite removal of the alcohol and its metabolites, thus reducing the duration of antidote administration. In the U.S. trials,[1–3] fomepizole-treated patients were dialyzed when plasma EG or methanol concentrations were >0.5 g/L. However, EG-poisoned patients treated with fomepizole prior to the onset of significant acidosis may not require hemodialysis.[4] Additionally, fomepizole may obviate the need for hemodialysis in selected methanol-poisoned patients, in the absence of neurological and ocular impairment or severe acidosis, on the basis of elevated serum methanol concentration alone.[5,6] The current criteria for dialysis are the presence of severe metabolic acidosis, electrolyte imbalances unresponsive to conventional therapy, renal failure, or deteriorating vital signs despite intensive supportive care.[7,8] For methanol poisonings, additional criteria are the presence of visual impairment or a plasma methanol concentration >0.5 g/L. In EG poisonings, initial serum glycolic acid concentration (>10 mmol/L) appears to be a good indicator for hemodialysis;[9] however, it is not readily available in most hospitals. Hemodialysis is unnecessary, regardless of EG level, if glycolic acid is ≤8 mmol/L in patients receiving antidote. When dialysis is indicated, continuous antidote infusion should be provided to compensate for its elimination. The traditional end-point of dialysis is a plasma concentration of the toxic alcohol <0.2 g/L, with resolution of acid-base disturbances and the osmolar gap. Continuous extracorporeal removal techniques including hemofiltration and hemodiafiltration are only indicated in case of cardiovascular impairment that may compromise conventional hemodialysis performance. All these extracorporeal removal techniques are invasive with significant risks of adverse effects. They are not universally available and difficult to use in case of epidemic alcohol poisonings. Moreover, if avoided by early fomepizole administration, admission to the intensive care unit may be limited to a relatively brief (24 h) period of observation. Therefore, we believe that it is worthwhile to confirm that fomepizole may obviate hemodialysis under certain conditions.[10] While comparing fomepizole with ethanol ± hemodialysis would be of interest, such a study has not been done and is unlikely to be done. The risks, costs and inconvenience of prolonged hospitalization if fomepizole alone is used, must be weighed against those of hemodialysis, if ethanol is preferred. *Conclusion:* When recommending fomepizole as an effective and safe first-line antidote for EG and methanol intoxications, the need for hemodialysis may be obviated in selected patients. While antidotal therapy without hemodialysis appears to be efficacious in a number of cases of uncomplicated poisonings, further experience is needed to clearly define the indications for associated hemodialysis. *References:* 1. Brent J. Fomepizole for ethylene glycol and methanol poisoning. N Engl J Med 2009; 360:2216–23. 2. Brent J, McMartin K, Phillips S, et al. Fomepizole for the treatment of ethylene glycol poisoning. Methylpyrazole for

Table 1. RR of clinical outcomes for DEG and GE exposures compared to EG

N = total number of cases	No - minor effects [95% confidence interval (CI)]	Moderate - severe effect including death (95% CI)	Acidosis (%)	Received 4MP (%)	Received HD (%)	Most Common Causative Agent
EG (N = 835)	77%	23%	116 (14%)	244 (29%)	113 (14%)	Antifreeze
	RR-1	RR-1				
DEG (N = 267)	93%	7%	9 (3%)	28 (10%)	3 (1%)	Brake Fluid
	RR-1.2 (1.03–1.39)	RR-0.33 (0.20–0.52)				
OGE (N = 845)	98%	2%	2 (0.2%)	7 (0.8%)	0 (0.0%)	Household Cleaning Products
	RR-1.27 (1.15–1.41)	RR-0.08 (0.05–0.14)				

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12. Challenges to Medical Systems by Terrorism with Chemical Warfare Agents

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Objective: The asymmetric use of chemical warfare agents against civilians and military personnel poses a pertinent threat towards the medical system. Among the substances classified by the chemical warfare convention[1] as chemical warfare agents, nerve agents (NA) and blistering agents are regarded as the most challenging compounds. Exposure may result from inhalation or percutaneously. The NA consist of highly volatile G-agents, e.g. sarin, and persisting V-agents, e.g. VX. Blistering agents, e.g. sulphur mustard (SM), are generally regarded as persisting substances. The development of signs and symptoms is quite fast (minutes) after inhalation and may be delayed (hours) after percutaneous absorption of V-agents or blistering agents. *Methods:* To overcome the challenge due to a possible terrorist attack with NA or SM, an overview of the present knowledge of therapeutic measures is given. *Results:* Prior to first aid, first responders and medical personnel have to be protected from contamination and victims from ongoing exposure. Removal from the contaminated area and fast undressing are regarded as effective methods to prevent further agent absorption. The most important toxic mechanism of NAs the inhibition of acetylcholinesterase (AChE), resulting in cholinergic crises and finally to death due to respiratory insufficiency. Early administration of atropine and an oxime is recommended. For this purpose, military personnel is equipped with autoinjectors for self and buddy aid. Stockpiling of autoinjectors and early use e.g. by trained first responders, may improve the response capacity to counteract terrorist attacks remarkably. The early administration of anticonvulsants, e.g. diazepam or midazolam, may be necessary. Further treatment has to be guided by the clinical course. Hereby, three different types of poisoning can be distinguished.[2] (i) Intoxication with NAs forming reactivatable NA-AChE complexes with short persistence of the NA in the body, e.g. inhalational sarin intoxication. In this situation effective oximes e.g. obidoxime or pralidoxime, may reactivate the inhibited enzyme promptly, thereby overcoming intoxication. In such cases, low atropine and anticonvulsant doses should be sufficient. (ii) Intoxications with NAs forming a reactivatable NA-AChE-complex with prolonged persistence of the NA in the body, e.g. percutaneous VX intoxication. In such cases, initially reactivated AChE may be re-inhibited by persisting agents and thus limiting the benefit of oxime treatment when the oxime concentration drops below a therapeutic level. Here, oximes should be administered as long as reactivation is possible, in combination with low atropine dosing according to demand, anticonvulsants in case of need and further symptomatic measures if appropriate. (iii) Intoxication with NAs resulting in NA-AChE-complexes that age rapidly or that cannot be reactivated by oximes sufficiently, e.g. inhalational soman or tabun intoxication. In such cases, victims do not benefit from oxime treatment. Here, higher atropine doses, anticonvulsants and further symptomatic therapeutic measures, e.g. artificial ventilation have to be applied. Alternative therapeutic approaches are under development, e.g. stoichiometric or catalytic scavengers, however neither of these are approved nor available at present. In contrast to NA, the toxic mechanism of SM consists in alkylation of proteins, DNA and RNA.[3] The clinical picture that develops several hours after acute SM exposure, is dominated by eye lesions, subepidermal blisters, respiratory tract damage and bone marrow depression. Unfortunately, in spite of decades of extensive research, no causal treatment is available to date. Thus, therapeutic measures have to be directed against signs and symptoms. Affected eyes should be rinsed, mydriatics and antibiotics applied according to demand. The administration of steroids may be considered. Affected skin needs appropriate nursing with frequent changes of wound dressing. Local antibiotics may prevent aggravation of skin infection in immuno-suppressed patients and may result in adequate, although delayed, wound healing. To counteract respiratory tract damage, mucolytics, codeine, steroids in combination with inhalation of moist air may be used. Pseudomembrane building and displacement may result in respiratory insufficiency and has to be controlled thoroughly. In spite of optimized treatment during the acute phase, late effects, e.g. skin effects, respiratory tract and lung damage as well as severe eye defects, frequently develop years after the acute exposure and remain a long term challenge to the medical system.[4] *Conclusion:* To counteract a terrorist attack with NA or SM clear understanding of therapeutic principles and preparedness are necessary. *References:* 1. Organisation for the prohibition of chemical weapons. Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on their Destruction. http://www.opcw.org/chemical-weapons-convention/download-the-cwc/2. Thiermann H, Szinicz L, Eyer P, et al. Lessons to be learnt from organophosphorus pesticide poisoning for the treatment of nerve agent poisoning. Toxicology 2007; 233:145–54. 3. Kehe K, Thiermann H, Balszuweit F. 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13. Chemical Hazards Emergency Medical Management: A New Online and Downloadable Information Resource for Planning for and Responding to Mass-casualty Incidents Involving Chemicals

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Objective: To be useful in disaster planning and response, an information resource must provide information that is authoritative, easy to apply, and sufficiently detailed to allow for application to a wide range of toxicants, situations, and populations. It needs to provide information that applies to the preparation, response, and mitigation phases of chemical disasters. It also needs to be user-friendly in the sense that it must organize the wealth of disaster-related planning and response details into a format that is easy for clinicians and planners to navigate both before and during a chemical emergency. *Methods:* The first author, in conjunction with the United States Department of Health and Human Services and the National Library of Medicine, examined the currently available Radiological Event Medical Management (REMM) module as a starting point for the development of a companion program, Chemical Hazards Emergency Medical Management (CHEMM). The basic organization of REMM was preserved, but the overall approach is being modified so that basic toxicological principles guide the organization and presentation of material. *Results:* The existing prototype of CHEMM provides introductory information to help educate users to approach chemical events from a toxicological perspective and incorporates easy-to-navigate but comprehensive tools that enable focused assessments of the type of chemical event, the nature of the agents involved, casualty presentation, probability-based estimation of likely agents based upon casualty signs and symptoms, decontamination, and management of patients, including special populations. Most importantly, CHEMM has been designed to be easily navigable by clinicians and nonclinicians both before and during a chemical emergency. *Conclusion:* CHEMM is poised to become a standard toxicological resource for chemical emergencies, including inadvertent releases and also terrorist events. *References:* 1. Bader JL, Nemhauser J, Chang F, et al. Radiation Event Medical Management (REMM): website guidance for health care providers. Prehosp Emerg Care 2008; 12:1–11. 2. Coleman CN, Hrdina C, Bader JL, et al. Medical response to a radiologic/nuclear event: integrated plan from the Office of the Assistant Secretary for Preparedness and Response, Department of Health and Human Services. Ann Emerg Med 2009; 53:213–22.

14. Hazmat Disasters - Prevention, Planning, Training

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Introduction: Industrial disasters with extensive damage to human health and the environment resulting from accidental explosions, fires and spills of large amounts of hazardous chemicals have frequently occurred in the last 80 years. The Seveso (Italy, 1976, dioxin)[1] and Bhopal (India, 1984, methylisocyanate)[2] disasters were two of the most famous. Human error, equipment failure, facility or transportation related factors very often are at the origin of the events.[3] *Discussion:* EPIDEMIOLOGY Chemical incidents are surprisingly common: the estimated number of all incidents in the world ranges from 100,000 to 500,000 per year, with 10 to 15 major Hazmat disasters.[4] HAZMAT RISK ASSESSMENT AND SCENARIO MODELLING An important part of any chemical disaster plan involves the survey of the area with the identification of hazardous chemical sites and transport routes, hazardous products and their chemical properties (concentration, physical state, vapor pressure, flammability and toxicity), evaluation of possible incident scenarios (risk assessment) and an estimation of the health and environmental impact of Hazmat incidents.[5,6] Various software programmes for scenario modelling use many inputs (substance, weather, topography) to predict and display the geographical extent of a hazardous atmosphere and its evolution. For flammable substances, the aerial impacts of fires, explosions and domino effects can be calculated as a function of thermal and overpressure levels.[7] HAZMAT DISASTER PLANNING Planning is fundamental for an effective response to a chemical incident. From the national to local levels, government and public authorities, resident population, emergency services (fire fighters, police, civil protection), environment agencies and local chemical industries need to set up the procedures necessary to ensure the effective response of any chemical incident. The public health sector (emergency medical services [EMS], hospitals, poison centers) must be fully involved and actively participate in the planning and preparedness process, including emergency plan development and implementation. This multi-disciplinary approach to a Hazmat disaster plan is the best way of achieving the necessary tasks that greatly enhance the resulting teamwork in an incident.[4,5,6] POISON CENTERS ROLE The poison centers must plan for chemical disasters and be prepared to provide detailed information about the toxic effects of the substance and

medical management (decontamination, diagnosis and treatment). The poison centers must be in constant communication by phone with the EMS, fire brigades, hospital emergency departments and health agencies.[5] HAZMAT RESPONSE First responders at the site of an incident are usually plant workers, fire brigades, police and EMS personnel. Communications should be activated within the agencies to mobilize the appropriate type and amount of resources. The command center near to the site is very important for controlling the incident and its evolution and establishing priorities (rescuers' safety and coordination, alerting population for indoor sheltering or evacuation). The dynamic boundaries of the hot (restricted) and warm (decontamination) areas affected by a release of hazardous materials must be delimited and the upwind, uphill, upstream cold (support) zone selected. Only trained and appropriately protected rescuers should enter the hot and warm zone. Personal protective equipment (PPE) are divided into four levels: from level A (fully encapsulating, chemical-gas-vapor-resistant suit and self-contained breathing apparatus) to level D (a work uniform with no respiratory protection and minimal skin protection). In the meantime police must establish security at the scene, ensure the area restriction and traffic control.[3] MEDICAL ACTIONS: Triage is begun by EMS personnel. In the field ABC and rapid classification of injury and color-coded tagging establish priorities for stabilization, treatment and evacuation of the injured patients. Victims should be rapidly moved out of the hot zone to the decontamination zone. Decontamination is always necessary prior to performing complete medical care except for victims exposed only to gas or vapors without skin or eye irritation. As soon as primary decontamination is completed, ABCDE (airway, cervical spine stabilization, oxygen administration, assisted ventilation, cardiac and BP monitoring, GCS evaluation and secondary decontamination) is quickly ensured. A complete evaluation of signs and symptoms is essential for recognizing traumas, burns and Hazmat toxic syndromes (irritant, simple and systemic asphyxiant, cholinergic, corrosive and hydrocarbon). Only at this point is specific treatment and the administration of the correct antidotes possible. Then the patients' dispatch to hospitals should begin and proceed, matching local and remote hospital resources with the patient load.[3] TRAINING Population, all emergency services and the local chemical plants' personnel need to be educated and trained (especially in recognizing the problem and for the correct use of PPE) in preparedness and response to chemical incidents, enabling them in a broad co-operative effort to resolve a Hazmat disaster. The effectiveness of theoretical training (i.e. AHLS) can be maximised with exercises: role-playing (case studies), functional emergency (simulation of activation, communications, integrated operations and decision making) and full-scale simulations (detailed scenario on the field with population participation). Exercise evaluation will enable the chemical incident plans to be regularly updated and improved.[5] *Conclusion:* The complexity of the response to Hazmat incidents and disasters is a never-ending, multi-disciplinary process based on prevention, planning and training which needs qualified people, continuous research, information and involvement of population and adequate financial resources. *References:* 1. Mocarelli P. Seveso: a teaching story. Chemosphere 2001; 43:391–402. 2. Broughton E. The Bhopal disaster and its aftermath: a review. Environ Health 2005; 4:6. 3. Ellenhorn MJ. Chemical disaster. In: Ellenhorn MJ, Schonwald S, Ordog G, et al, eds. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, USA: Williams & Wilkins, 1996:1236–12. 4. Coleman G, Palmer S, eds. Public health and chemical incidents guidance for national and regional policy makers in the public/environmental health roles. WHO Collaborating Centre for an International Clearing House for Major Chemical Incidents, University of Wales Institute, Cardiff, 1999:12–13. 5. Organization for Economic Cooperation and Development (OECD) Environment Monograph No. 81. UNER IE/PAC Technical Report No. 19, Health aspects of chemical accidents. Guidance on chemical accident awareness, preparedness and response for health professionals and emergency responders. Paris, 1994. 6. Waeckerle JF. Disaster planning and response. N Engl J Med 1991; 324:815–21. 7. El Harbawi M, Mustapha S, Choong TSY, et al. Rapid analysis of risk assessment using developed simulation of chemical industrial accidents software package. Int J Environ Sci Tech 2008; 5:53–64.

15. Poison Center Data: Complete or Completely Inaccurate? How to Improve Accuracy in Data Recording

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Objective: Poison center chart data are analyzed for a variety of purposes. These include real-time event surveillance, poisoning demographics, severity of exposure, procedures and treatments recommended and/or used and their efficacy, and outcomes. Call-takers document using code numbers for substances, check-off boxes, drop-down menus, and write narrative to describe cases. We sought to increase call-taker accuracy in recording poison center data using a newly created continuous quality improvement (CQI) method. *Methods:* We retrospectively analyzed our regional poison center's human exposure case records created during nineteen consecutive months. One hundred charts from each month were randomly selected to review for errors in four areas: exposure reason, route of exposure, clinical effects, and treatments/therapies. An error was identified for exposure reason and route if the selected code did not match the narrative. Similarly, if a clinical effect or treatment/therapy was mentioned in the narrative and the corresponding box was not checked, an error was recorded. Call-takers received periodic feedback of coding and documentation errors to encourage improvement. *Results:* We identified 566 errors contained within 23% of charts (442/1900). Of those, 35% were attributed to discordance between treatment/therapy identified in the narrative section and not checked off correctly elsewhere on the chart. Clinical effects (29.2%), exposure reason (28.2%), and route of exposure (7.6%) made up the remaining errors. *Discussion:* To assist in developing short-term and long-term public health care strategies, recent emphasis has been placed on providing accurate and complete poison center data to improve real-time poisoning event surveillance and trends analyses. Since implementing this CQI project, call-taker charting errors decreased from 66 in the first month to 17 in the last. Periodic feedback and group discussion provided to call-takers allowed for correction of inaccurate data charting practices during the study period and was felt to be the key element in leading to a gradual improvement in accuracy. *Conclusion:* This CQI tool has proven to be an effective strategy in reducing our reporting errors, and improving our poison center data accuracy. This model of data CQI may be a useful tool for other poison centers to improve poison center data recording.

16. Poisons Centres' Data for Expert Judgement within Classification, Labelling and Packaging Regulation: Solid Household Automatic Dishwashing Products do not Cause Serious Eye Damage

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Objective: The European Regulation on Classification, Labelling and Packaging (CLP, 1272/2008) entered into force in January 2009. Herein, application of a new calculation method results in the classification "serious eye damage" (hazard category 1) and labelling with symbol GHS05 (corrosion) for many products that had been labelled as "irritant" before, e.g. many solid household automatic dishwashing products (ADW). Labelling could lead to inappropriate medical treatment if risks indicated on the label do not reflect real risks known from experience in clinical toxicology. CLP Annex I 1.1.1 indicates that expert judgement should be applied "where weight of evidence determinations are needed" to achieve an appropriate classification and labelling of products. Questions of the study: 1. Do ADW cause severe or lasting eye lesions? 2. What is the correct classification and labelling for ADW? 3. Are poisons centres' (PC) data suitable for expert judgement? *Methods:* Retrospective study collating and evaluating human eye exposures with ADW recorded by all 11 PCs in Austria, Germany and Switzerland between 1998 and 2007 (MAGAM study). *Results:* Among 1,841,438 human cases recorded in the study centres 16,755 (0.9%) exposures to ADW were identified. In 117 of these cases (0.7% of ADW exposures) eyes have been exposed including 55 eye exposures in children (<7 years). Poisoning severity in these cases: no symptoms: 28; minor: 75; moderate: 1; severe or lethal: 0; unknown: 13. In 12 cases followed up no indication of incomplete recovery was found. *Conclusion:* 11 PCs did not record any case of severe or lasting eye damage after local exposure with ADW in a population of about 100 million inhabitants in 3 European countries within 10 years. Critical evaluation of all cases gave no indication of serious eye damage in any of these cases. Thus, due to the dataset evaluation in this study hazard category 2, "eye irritation" with symbol GHS07 (exclamation mark) seems to be an adequate classification and labelling for solid household automatic dishwashing products to avoid unnecessary (and risky) medical treatment in many cases. The study shows that PC data can provide a solid basis of expert judgement for CLP.

17. The Feasibility of Multicentre Data Collection on Poisoning in Europe, using Paraquat as an Example

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Objective: Paraquat has been used as herbicide worldwide since 1962. The aim of this study was to collect adverse health incident data to a common standard in Europe, using paraquat as model substance. *Methods:* Poisons centre-based prospective multicentre cohort study in 9 European countries where paraquat was marketed during 2006–2008. In the first months of 2006 data were collected in a retrospective pilot study. Patient and exposure characteristics were recorded and likelihood of exposure, symptoms, severity, causality, and outcome were assessed. Completeness of case report forms (CRF) and adherence to the study protocol were evaluated. *Results:* Total reported cases n = 419 (from Greece 97, Spain 93, Portugal 84, United Kingdom 60, France 38, Italy 17, Belgium 6, Germany 12, Netherlands 8, Slovakia 3, Cyprus 1). The percentage of completed data fields in the case report forms is shown in Table 1. The highest rate of reporting had the route of exposure with information present in

Table 1. Completeness of Case Report Forms (overall and range by centres)

Data field	% complete	lowest	highest
Route of exposure	98.8%	91.7%	100%
Sex	98.3%	85.7%	100%
Likelihood of exposure	98.3%	50.0%	100%
Results of analytics*	98.2%	50.0%	100%
Age group	98.1%	91.7%	100%
Level of documentation	97.4%	50.0%	100%
Time of exposure	95.0%	75.0%	100%
Methods of analytics*	94.1%	25.0%	100%
Incident type	93.3%	50.0%	100%
Analytics performed (yes/no)	93.3%	81.7%	100%
Severity	93.3%	75.0%	100%
Brand name	91.4%	50.0%	100%
Description of treatment	91.4%	0%	100%
Time of call	90.2%	0%	100%
Age (years)	79.7%	25.8%	100%
Circumstances of exposure	70.6%	37.6%	100%
Outcome	58.5%	0%	100%
Manufacturer**	55.6%	0%	100%
Dose or concentration	37.7%	0%	100%

*only, if analytics were done
**information deliberately withheld by the Madrid Poisons Centre

98.8% of CRFs; the lowest value for a single centre was 91.7%. Poor reporting rates (<80%) had age (in years), the description of the circumstances of exposure, final outcome, and the ingested paraquat dose or concentration exposed to. The lack of this information was due to difficulties in obtaining it from the caller, or to the failure of getting follow-up information. Only 17.8% of initial notifications of a case in the 2007–2008 period were within 3 days after the call as stipulated by the study protocol. *Conclusion:* It is feasible to prospectively collect data from different poisons centres using predefined criteria. Poisons centres had difficulties in collecting information about circumstances of exposure, age of the patient, and medical follow-up. Most cases were reported after a delay.

18. Normoinsulinemic Hypoglycemia in Venlafaxine Poisoning

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Objective: Venlafaxine, a structurally novel antidepressant, is a potent combined neuronal serotonin and noradrenaline reuptake inhibitor and weak inhibitor of dopamine reuptake. Venlafaxine poisoning may result in serotonin syndrome, coma, seizures, rhabdomyolysis, arrhythmias, and renal and liver failure. There is only one report of hypoglycemia after venlafaxine overdose that was explained by an increased endogenous insulin level. In this case we present prolonged hypoglycemia in venlafaxine poisoning with normal insulin levels. *Case report:* A 42-year-old woman with depression ingested 9,000 mg of venlafaxine in a suicide attempt. On arrival at the ED 4 hours after ingestion she was somnolent and had mydriasis, tremor, tympanic temperature 36.5 °C, pulse 130/minute and blood pressure 115/60 mmHg. Gastric lavage was performed and activated charcoal was given, immediately after which she had a grand-mal seizure. Gut decontamination with polyethylene glycol was performed. The initial serum glucose level was 2.6 mmol/L and potassium 3.2 mmol/L; all other laboratory results were within normal limits. A continuous infusion of 10% glucose with potassium was started at 250 mL/h. Intermittent hypoglycemia (0.9–3.2 mmol/L) with neurological signs was recorded 7 times during subsequent hospitalization, the last episode being detected 40 hours after venlafaxine ingestion. Serum creatine kinase increased to 82 µkat/L and myoglobin to 531 µg/L, but renal function remained unaffected. A toxicology analysis of serum by LC-MS/MS revealed 14.7 mg/L of venlafaxine twelve hours after ingestion (therapeutic range 0.07–0.27 mg/L). Afterwards serum venlafaxine concentration decreased with a prolonged half-life of 15 hours (at 5 hour therapeutic doses). No ethanol or other medications were found. The subsequent insulin measurement by immunoradiometric assay revealed plasma insulin levels of 23, 26, 17 and 3 mU/L in plasma samples taken 12, 18, 24 and 40 hours after ingestion, respectively (normal levels 2–29.1 mU/L). C peptide was normal as well. *Conclusion:* Venlafaxine poisoning can present normoinsulinemic hypoglycemia lasting 40 hours. The pathogenic mechanism is unclear, but inappropriately serotonin increased release of insulin up to upper normal levels, insulin sensitizing effects and enhanced cellular glucose entry in serotonin syndrome could be some of the reasons. In venlafaxine poisoning immediate glucose measurement is essential and prolonged hypoglycemia can be expected.

19. Naltrexone-Induced Severe Opioid Withdrawal Treated with Intravenous Fentanyl Infusion

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Objective: Naltrexone-induced opioid withdrawal can be prolonged and severe. No approach to treatment has been evaluated and there is a paucity of data related to treatment. We present 2 cases to demonstrate one effective approach to treating naltrexone-induced opioid withdrawal. *Case series:* Case 1: A 62 year old woman with opioid dependence presented to the hospital in opioid withdrawal 3 hours after ingesting naltrexone 50 mg prescribed by her dermatologist for itching related to a skin disorder. She had no improvement of her nausea, vomiting, diarrhea, severe body and joint pain, and yawning after receiving 200 mcg of intravenous fentanyl, 2 mg hydromorphone, 8 mg morphine, and 1 mg lorazepam. She was placed on an intravenous infusion of fentanyl, titrated to her withdrawal symptoms. In the ICU, her fentanyl infusion was as high as 175 mcg/hour. She was closely monitored for respiratory depression and rigid chest syndrome and the infusion was titrated off approximately 36 hours after ingestion. Case 2: A 54 year old man on opioids for cancer-related pain presented to the ED with constipation for 7 days and diffuse abdominal pain. He was treated with IV fluids and admitted to the hospital after a CT scan and laboratories did not reveal the etiology of his pain. While on the inpatient service, a trial of oral naloxone was initiated to relieve his constipation. Mistakenly, he was treated with naltrexone and developed severe opioid withdrawal. There was no response to a total of 30 mg intravenous morphine. The patient was moved to the ICU and started on an intravenous fentanyl infusion. The infusion was as high as 100 mcg/hr and he was closely monitored for respiratory depression and rigid chest syndrome. The infusion was discontinued approximately 24 hours after the ingestion. *Conclusion:* Naltrexone is an opioid antagonist with a high affinity for the mu receptor. Fentanyl is a synthetic opioid with approximately 100 times more potency than morphine. Its short duration of action makes it ideal for intravenous titration. Intravenous fentanyl infusion is a safe and effective treatment for naltrexone induced opioid withdrawal. High doses may be required and therefore a closely monitored setting recommended.

20. Venlafaxine-Induced Rhabdomyolysis

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Objective: Venlafaxine, an antidepressant drug, inhibits its CNS serotonin and norepinephrine neuronal uptake. In overdose, venlafaxine has been reported to cause rhabdomyolysis. *Case report:* A 46 year old man with a history of bipolar depression was admitted following suicidal ingestion of 100 tablets (1 tablet = 75 mg; total dose = 7.5 g) of venlafaxine twelve hours before hospital presentation. There was no history of seizures. Findings on admission included Reed II coma, fixed equal mydriasis, muscular hypertonia, bradypnoea, hypoventilation, hypertension (BP=140/80 mmHg), tachycardia (130 b/min.), fever (39 °C) and dark coloured urine. Pulmonary radiography revealed aspiration pneumonia. Initial abnormal laboratory findings were myoglobin > 1000 ng/mL, CK 6452 U/L (normal range 55–170 U/L), and LDH 645 U/L (normal range 313–618 U/L). The therapy initiated was ventilatory support, sedation with benzodiazepines, intravenous fluid repletion and alkaline diuresis, and broad spectrum antibiotics. Gastric lavage was performed and a 50 g dose of activated charcoal was administered. Toxicology analysis by GS/MS was positive for venlafaxine in urine. Twenty-four hours post-admission, CK had elevated to > 20,000 U/L along with LDH, hepatic enzymes and amylase, but after 48 hours began to decrease. Renal function remained normal throughout. The outcome was favourable. The patient was weaned from ventilator support after 5 days, regained consciousness at 7 days, and correction of hepatocytolysis and rhabdomyolysis syndromes occurred at 11 days. Pulmonary healing and discharge occurred after 16 days. *Conclusion:* Rhabdomyolysis, resulting from serotonin toxicity and acute muscle injury, complicates venlafaxine poisoning and prolongs the hospital stay.

21. Ventricular Fibrillation and Tachycardia Provoked by Vagal Maneuvers in Ibogaine Poisoning with Prolonged QT-interval

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Objective: Ibogaine is a hallucinogenic indole alkaloid used in alternative medicine to treat addiction, causing QT-interval lengthening and ventricular tachyarrhythmias what might be due to autonomic nervous dysregulation and vagal dominance after high doses. We present prolonged QT-interval and ventricular tachyarrhythmias induced by vagal maneuvers after ibogaine ingestion. *Case report:* A 33-year-old man was given ibogaine by an alternative healer to alleviate drug craving after two days of cocaine, heroin and methadone abstinence. After 30 minutes he became lightheaded and lost consciousness while trying to urinate. His breathing was shallow, pulses not palpable and resuscitation was started. On arrival of the physician 6 minutes later the patient had ventricular fibrillation (VF) that was defibrillated. On admission his GCS was 15, pulse 60/min, blood pressure 110/60 mmHg and respiratory rate 20/min. Serum electrolytes were normal and ECG showed prolonged QTc-interval of 460 msec. During the first 10 hours he developed two VFs, one after miction, which were defibrillated as well. Afterwards amiodarone was started and sinus bradycardia 40–60/min, further QTc-interval prolongation, ventricular extrasystoles, bigeminy and one VF appeared. Amiodarone was stopped 32 hours after ingestion, but QTc-interval lengthening continued up to 593 msec. He developed three ventricular tachycardias (VT) between 36 and 46 hours, each time while trying to urinate or defecate. Bicarbonate and magnesium had no effect. Forty-eight hours after ingestion amiodarone was reintroduced and VT/VF did not reappear, but ventricular extrasystoles persisted for an additional 12 hours. Amiodarone was

stopped on the 4th day. Sinus bradycardia persisted till the 6th day and QTc-interval normalized on the 9th day. Toxicological analysis by GC/MS confirmed methadone and ibogaine on arrival. Ibogaine was detected in the patient's blood at 9 days. Structural heart disease was excluded by echocardiography, coronography and MRI. Genetic long QT-interval syndromes were excluded. On discharge Holter monitoring and electrophysiology study were normal. *Conclusion:* Ibogaine prolongs QT-interval and causes VF/VT that might be provoked by vagal manoeuvers such as miction or defecation. Amiodarone should be used cautiously in ibogaine poisoning as it additionally lengthens QT-interval. In ibogaine poisoning patients should be monitored, vagal manoeuvers prevented and lidocaine considered for ventricular tachyarrhythmias.

22. Zotepine-Induced Acute Respiratory Distress Syndrome

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Background: Acute respiratory distress syndrome (ARDS) is a severe form of acute lung injury. The definitive mechanism remains unclear. Few antipsychotics or antidepressants had been reported to induce ARDS in overdose. Zotepine is a dibenzothiepine atypical antipsychotic for schizophrenia with few side effects. Here, we report a case of zotepine overdose complicated with ARDS and successfully treated with extracorporeal membrane oxygenation (ECMO). *Case report:* A 44-year-old female was intoxicated with 3000 mg of zotepine and 1000 mg of trazodone. She received endotracheal tube insertion with mechanical ventilation due to respiratory failure on day 2 in a local hospital. She presented to our emergency unit with ARDS on day 3. She received ECMO therapy due to hypoxia despite of 100% oxygen therapy on day 4. She was successfully weaned from ECMO 8 days later and discharged in a stable condition after 21 days of hospitalization. *Conclusion:* ARDS has been described in a few cases of tricyclic antidepressant or selective serotonin reuptake inhibitor overdose. Endothelial and/or epithelial cell damage and increased permeability of the alveolar /capillary barrier have been suggested to be the probable mechanism. High dose zotepine intoxication might also induce acute lung injury and needs aggressive management.

23. Enhanced Elimination in Sustained-release Potassium Chloride Poisoning - A Case Series

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Objective: To describe the management of three episodes of sustained-release potassium chloride (KCl) poisoning presenting in an adult and a child involving haemodialysis and whole bowel irrigation. *Case series:* Case 1/episode 1 - 42 year old woman presented within 90 minutes of ingesting forty tablets of Slow-K (Novartis, potassium chloride 600 mg; K^+ 8 mEq). She was alert and co-operative with a potassium level of 5.5 mmol/L, pH 7.42 and ECG showing peaked T waves. X-ray showed around 30 radio-opaque tablets in the upper abdomen. She was commenced on whole bowel irrigation with polyethylene glycol at 2 litres per hour (for 15 hours) via nasogastric tube. A total of 25 tablets of KCl were counted in the effluent and her potassium level peaked at 5.7 mmol/L. The patient suffered no sequelae of overdose and was discharged the following day. Case 1/episode 2 - the same woman presented 6 months later with ingestion of 100 tablets of Slow-K. At 5 hours post-ingestion, her abdominal x-ray revealed only a few tablets and a peak potassium level of 8.5 mmol/L; pH 7.38. Along with standard hyperkalaemia management, she was commenced on high-flux haemodialysis. Her potassium level declined to normal levels and she was discharged the following day. Case 2 - a 6 year old boy, with a history of autism, was brought into a small peripheral hospital after vomiting 50 tablets of Slow-K. A further 150 tablets were missing and thought to have been ingested by the child. Abdominal X-ray showed over 50 tablets in the stomach. With a potassium level of 7.6 mmol/L, pH 7.30 and electrocardiograph signs of hyperkalaemia, he was resuscitated with sodium bicarbonate, insulin/dextrose and calcium chloride. Whole bowel irrigation was not attempted at this hospital. The boy was retrieved to a tertiary paediatric intensive care unit and underwent urgent haemodialysis (total 9 hours). His potassium level remained below 4.5 mmol/L for the remainder of his admission. *Conclusion:* Sustained-release KCl ingestion can have disastrous consequences if not recognised early and treatment instituted to remove the total body burden of potassium. Extra-corporeal methods of elimination can be life-saving in the face of cardiotoxicity secondary to hyperkalaemia.

24. A Study of Outcomes of Steroid Therapy in Severe Acetic Acid Poisoned Patients

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Objective: The ingestion of 70% solution of acetic acid is still wide spread in Russia both in accidental and suicidal cases. The average level of morbidity for the last 8 years in the Sverdlovsk region was 13.8 per 100,000 people with the mortality rate of 1.23 per 100,000. The aim of this study was to define the influence of steroid therapy on the mortality rate and frequency of strictures. *Methods:* Case notes of patients admitted to the Sverdlovsk Regional Toxicological Centre during January 2006 - March 2009 were reviewed. Significance of differences was estimated with t and z criteria. *Results:* Severe acetic acid poisonings with hemolysis and ulcerative-necrotic injury of the digestive tract were defined in 112 of 261 cases. The average dosage was 96.1±12.9 g/L. Kidney failure developed in 47.3% of cases, bleeding in 51.8%. Fifty-eight of 112 patients died but 16 died of shock and bleeding during the first 3 days, and for this reason they were excluded from the analysis. The remaining 96 patients were divided retrospectively into 2 groups as follows: the first group consisted of 35 patients, 23 of whom got prednisolone for 2.7±0.4 days on average and another 12 who did not receive any prednisolone; the second group consisted of 61 patients who got prednisolone for longer (10.9±5.6 days on the average). In the first group 12 patients died (34.3%) and in the second group 30 (49.2%) patients died, but the difference was not significant (z=1.2, p=0.23). Kidney failure requiring hemodialysis developed in 17 patients of the first group (35.3% of them died), and in 23 patients of the second group (73.9% of them died). There was significant difference (z=2.12, p=0.034) between the mortality rate of the first and second group patients who developed kidney failure. Esophageal or pyloric strictures developed during the first month in 30.4% surviving patients of the first group and in 35.5% of the second one. The difference was not statistically significant. *Conclusion:* Long term steroid therapy in severe acetic acid poisoning can increase the mortality rate but does not decrease the development of strictures.

25. Fluoxetine and 3,4-Methylenedioxymethamphetamine Induced Serotonin Syndrome Responsive to Propofol Therapy

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Objective: To describe propofol treatment for severe serotonin syndrome. *Case report:* A 27 year old female presented with agitation, seizure, and altered mental status after ingesting 3,4-methylenedioxymethamphetamine (MDMA) and two 20 mg fluoxetine tablets. Vital signs were rectal temp 102 F, heart rate 201 bpm, respiratory rate 32 bpm, blood pressure 128/67 mm Hg. Physical exam was significant for diaphoresis, dilated unreactive pupils (8 mm), diffuse rigidity, spontaneous clonus, ping-pong-like eye movements, and depressed mental status. Six milligrams of lorazepam had minimal effect on her tachycardia, agitation, or muscular hypertonicity. Following intubation for airway protection (etomidate and vecuronium were used) she was sedated with propofol; infusion was maintained between 45–50 mcg/kg for 6 hours while awaiting transport to a facility that had cyproheptadine. During this time her heart rate decreased to 100 bpm and her rigidity improved significantly. Fluoxetine, an inhibitor of CYP2D6, and MDMA, metabolized by CYP2D6, are both associated with serotonin syndrome individually.[1] Traditional treatment of serotonin syndrome includes benzodiazepines for mild cases and cyproheptadine for severe cases. Murine studies have demonstrated anxiolytic properties of propofol;[2,3] this may be mediated by 5-HT inhibition.[3] Human reports of propofol mediated anxiolysis exist and others demonstrate improvement of serotonin syndrome after propofol treatment.[4,5] *Conclusion:* Our case demonstrates that muscular hyperactivity and autonomic excitability can be mediated with propofol infusion. Propofol may be an important adjunct to 5-HT antagonists and an effective treatment for patients at centers that do not carry cyproheptadine. *References:* 1. Boyer EW, Shannon M. The serotonin syndrome. NEJM 2005; 352:1112–20. 2. Kurt M, Bilge SS, Kukula O, et al. Anxiolytic-like profile of propofol, a general anesthetic, in the plus-maze test in mice. Polish J Pharm 2003; 55:973–7. 3. Matsuo M, Ayuse T, Oi K, et al. Propofol produces anticonflict action by inhibiting 5-HT release in rat dorsal hippocampus. Neuroreport 1997; 8:3087–90. 4. Ganetsky M, Babu KM, Boyer EW. Serotonin syndrome in dextromethorphan ingestion responsive to propofol therapy. Ped Emer Care 2007; 23:829–31. 5. Borgeat A, Wilder-Smith OH, Suter PM. The nonhypnotic applications of propofol. Anesthesiology 1994; 80:642–56.

26. A case of Severe Ethylene glycol Poisoning: Late Though Successfully Treated

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Objective: We describe a case of severe ethylene glycol (EG) poisoning treated with fomepizole and hemodiafiltration (CVVHDF). *Case report:* A 39-year-old unconscious man with a previous history of alcoholism was found in his car. At the local hospital admission oral intubation and mechanical ventilation were performed; cerebral CT was negative; no diagnosis was formulated. He was then transferred to the reference-hospital ICU. Initial laboratory data revealed pH = 6.71, pCO_2 = 26.6 mmHg, HCO_3^- = 4.5 mmol/L, BE = –32.4 mmol/L, anion gap = 37 mEq/L, osmolal gap = 21 mOsm/L; K^+ = 6.6 mEq/L; ethanol 0.12 g/L. $NaHCO_3$ 450 mEq + 200 mEq were administered. Suspected EG poisoning was confirmed by EG blood level (131.5 mg/dL). Fomepizole 15 mg/kg was immediately administered and CVVHDF was performed. During the following three days fomepizole 10 mg/kg were administered every 8 hours. CVVHDF was repeated every day during the following 6 days. On day 4, EG plasma level was <4 mg/dL and fomepizole administration was stopped; on day 5 the patient was extubated: he showed no neurological sequelae, no metabolic acidosis, no electrolyte imbalances and EG=1.5 mg/dL. The patient finally confessed he had ingested antifreeze (about 200 mL containing EG 95%) and spirits in a suicide-attempt. Renal failure required additional CVVHDF for 3 more days. On day 7 the patient presented pneumonia and prolonged his ICU stay. On day 16 he was transferred to a nephrology ward. On day 30 he was discharged home and presented slight renal failure not requiring hemodialysis. *Conclusion:* Despite the fact that the patient's clinical condition was severe and his ICU admission was delayed, aggressive treatment with

fomepizole and hemodialysis was determinant in obtaining the patient's recovery.

27. Benzodiazepine Resistant Sympathomimetic Toxidrome Responding to Pentobarbital

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Objective: Benzodiazepine resistant alcohol withdrawal can respond to barbiturates. Sympathomimetic toxidromes from amphetamines are treated with increasing doses of benzodiazepines until vital signs normalize and agitation resolves. A case of lisdexamfetamine dimesylate ingestion in a two year old was resistant to large doses of benzodiazepines but responded to pentobarbital. No prior cases of benzodiazepine resistant sympathomimetic toxidromes have been described. *Case report:* A two year old boy weighing 14.4 kilograms, in good health, taking no medications, was found with an open bottle of 50 mg lisdexamfetamine dimesylate tablets used to treat attention deficit disorder in his older brother. Three tablets (150 mg) were missing. Fifteen minutes later, his mother described the child as confused, dazed, and agitated. He was taken to a community hospital emergency department. Vital signs were pulse 170/minute, blood pressure 147/97, and temperature 36.8C. He was hyperactive with dilated pupils. There was no improvement with IV administration of diazepam 0.8 mg, midazolam 1.5 mg and 2.0 mg, lorazepam 1.0 mg, 1.0 mg, and 6 mg, and midazolam infusion titrated to 6 mg/hour. He was transported to a pediatric intensive care unit where he received IV injections of a total of lorazepam 4 mg, diazepam 4 mg, and midazolam 26 mg, and midazolam infusion titrated to 7 mg/hour over a ten hour period without improvement. Pentobarbital 14.4 mg IV was given with immediate resolution of agitation. Vital signs normalized. He remained calm with normal vital signs for 7 hours. The midazolam infusion was tapered to zero. He became agitated again and received an additional IV bolus of pentobarbital 14.4 mg with good response. Midazolam infusion was reinstituted and titrated to 4 mg/hour. Seven hours later agitation, tachycardia, and agitation returned but resolved after a third dose of pentobarbital 14.4 mg. No further medications were needed, and the child was discharged in good health after a period of observation. *Conclusion:* Lisdexamfetamine dimesylate in a child resulted in a sympathomimetic toxidrome that did not respond to benzodiazepines. Pentobarbital immediately terminated the toxidrome. Sympathomimetic toxidromes resistant to benzodiazepines may respond to barbiturates like benzodiazepine resistant alcohol withdrawal.

28. Acute Intoxication with Valproic acid, Treated with Haemodialysis/Haemoperfusion in Series - Case Report

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Objective: Valproic acid, due to its properties such as low volume of distribution, low molecular mass (144 kDa), protein binding diminishing simultaneously with increase in drug concentration, is amenable to different methods of extracorporeal elimination.[1,2] *Case report:* A 16 year old female patient was admitted to the ward after suicidal ingestion of an unknown amount of valproic acid (Depakine Chrono). On admission she was fully conscious but negative, refusing any cooperation, without significant abnormalities on physical examination. She gradually deteriorated. After 8 hours of observation she was comatose, developed metabolic acidosis and hypotension. It was associated with increase in valproic acid level in blood to 855 microgram/mL. There were no other expected abnormalities, particularly thrombocytopenia or laboratory features of liver injury. Platelets count was $508x10^3$/microliter. Given the clinical deterioration, high valproate concentration and lack of thrombocytopenia we decide to combine haemodialysis with haemoperfusion on charcoal column, performed simultaneously in series. Blood samples were taken during the procedure before dialyser, between dialyser and column, and after column. Extraction ratio on dialyser diminished from 0.386 to 0.350, whereas extraction ratio on column decreased from 0.756 after 1 hour to 0.119 after 4 hours when the procedure was ended. Extraction ratio for total process decreased from 0.850 after 1 hour to 0.427 at the end of procedure. During elimination significant clinical recovery was noted, associated with decrease in xenobiotic concentration in blood to 168 micrograms/mL, with half time of elimination of 2.2 hours during extracorporeal elimination. The patient did not develop any significant complication during the procedure or after it. Rebound increase of valproic acid level was also absent. *Conclusion:* Addition of haemoperfusion to haemodialysis appeared to increase significantly the effectiveness of extracorporeal elimination of valproic acid and to be relatively safe in selected patients. *References:* 1. Sztajnkrycer MD. Valproic acid toxicity: overview and management. Clin Toxicol 2002; 40:789–801. 2. Thanacoody RHK. Extracorporeal elimination in acute valproic acid poisoning. Clin Toxicol 2002; 47:609–16.

29. Seizures in Acute Poisoning in Children - 5 Year Study

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Objective: To study the prevalence of an acute life-threatening situation: seizures, in acute poisoning in children. *Methods:* We made a retrospective study of acute poisoning cases admitted to a pediatric poisoning department during a five year period. The following criteria were taken into consideration: etiology of poisoning, type of poisoning, age, severity of poisoning. *Results:* 3687 patients with acute poisoning were admitted to our department between November 1st 2004 and October 30th 2009. Seizures were noted in 47 patients representing 1.25% out of the total number of poisonings. The acute poisonings resulting in seizures were the following: cholinesterase inhibiting pesticides: 18 cases, Dentocalmin (local anaesthetic used in stomatology which contains in 10 mL: lidocaine 2 g, menthol 2 g, phenol 2 g) 14 cases, carbon monoxide (CO) 7 patients, pyrethroids 3 cases, isoniazid 3 cases, tricyclic antidepressants 2 cases. In organophosphate and carbamate poisoning the seizures appeared later in the course of poisoning while in all the other situations they were noted at the onset of the poisoning, as one of the first symptoms. The age range was the following: up to 1 year: 5 cases, 1–5 years: 12 cases, 6–12 years: 12 cases, 13–18 years: 18 cases. There were 6 intentional poisonings and 41 accidental. Deaths were registered in 6 cases (2 patients with diazinon poisoning, 2 patients with carbofuran, 1 patient with CO and 1 patient with Dentocalmin poisoning). *Conclusion:* Although not very frequent, seizures represent one of the major life-threatening situations in acute poisoning in children (the rate of deaths being 2.8% compared to mortality in pediatric poisoning of 0.26%). The most frequently implicated agents in producing seizures in acute poisoning in children in our study were organophosphates and carbamates followed by Dentocalmin and carbon monoxide. *References:* Olson KR. Emergency Evaluation and Treatment. In: Olson KR. Poisoning and Drug Overdose. 4th ed. New York, USA: McGraw-Hill 2004: 22–32.

30. A Case of Successful Therapy in Acute Valproic Acid Poisoning in a Child Using Hemodiafiltration

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Objective: Extracorporeal detoxification is not used often in poisoning treatment in children of an early age, so the description of a case of successful therapy in a child with poisoning with the anticonvulsive drug Depakin (valproic acid) by hemodiafiltration is of certain interest. *Case report:* A girl aged 11 months, weight 9 kg 800 g was admitted to the ICU of Moscow Children Poisoning Treatment Center 24 hours after she had ingested an unknown number of Depakin tablets. On admission her condition was critical: she was in deep coma, had muscle hypotonia, hyporeflexia and seizure activity. Blood pressure was 70/35 mmHg, pulse rate146 bpm. Blood analyses showed mild metabolic acidosis with pH 7.25 and BE -8,5 mEq/L, decreased levels of potassium to 3.1 mmol/L, sodium to 129 mmol/L, calcium to 0.8 mmol/L, increase in lactate levels by 1.5 times, AST by twice. Depakin concentration in blood plasma was on admission 131.99 microgram/mL. The treatment included forced diuresis and infusion of hydroxyethyl starch 6% solution. To intensify detoxification continuous veno-venous hemodiafiltration was carried out for 7 hours by the system for extracorporeal blood purification with the volume of hemocartridge of 47 mL. The speed of hemoperfusion was 50 mL/min. After 5 hours of hemodiafiltration the child's conscious level improved to somnolence with no signs of seizure activity. Blood pressure registered at 85/50 mmHg, pulse rate 129 bpm, acid-base and electrolyte balances were practically normal with pH 7.36 and BE 1.2 mEq/L, levels of potassium 3.9 mmol/L, sodium 138.5 mmol/L, calcium 1.2 mmol/L. Depakin concentration in blood plasma after hemodiafiltration decreased to 37.76 microgram/mL. The child started to open her eyes after her name was called. *Conclusion:* A small volume of hemocartridge and slow speed of hemoperfusion makes possible the usage of hemodiafiltration in children of an early age, and it could be regarded as an effective method of therapy in severe poisoning by valproic acid.

31. Continuous Venovenous Hemodiafiltration in Acute Theophylline Overdose - a Case Report

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Objective: In 2000 Okada et al reported on the application of continuous venovenous hemodiafiltration (CVVHDF) in chronic theophylline overdose.[1] To the best of our knowledge there are no reports in the medical literature about the use of CVVHDF in acute theophylline intoxication. *Case report:* A 31-year old male who ingested about 7.5 g of slow-release theophylline, and ethanol presented. At admission the patient was conscious, with good verbal response, mildly agitated. The heart rate was 124 b/min, blood pressure 130/70 mmHg, respiratory rate 25 b/min. Blood glucose level was 135 mg/dL, potassium 3.1 mmol/L, theophylline 95 mg/L, and ethanol 2.9 g/L. Despite aggressive supportive treatment, the patient's condition deteriorated over the next six hours with increasing confusion, agitation, tremor, tachycardia (170 b./min.), and hypotension (80/40 mmHg). Theophylline level increased to 165 mg/L, blood glucose level to 279 mg/dL and potassium level decreased to 2.7 mmol/L. Metabolic acidosis with pH 7.31; HCO_3 14.6 mmol/L, base deficit -10.7 mmol/L, and lactate level 8.0 mmol/L was observed. The decision to use continuous renal replacement therapy was taken. A hemodialysis catheter (13.5 F, 24 cm) was inserted into the right femoral vein and CVVHDF (Prisma M 100 Pre Set) was started. The treatment parameters were: blood flow 150 mL/min, dialysate 2500 mL/h, replacement 1000 mL/h, and fluid removal 100 mL/h. Anticoagulation was achieved with continuous hep-

arin infusion in dosage of 750 U/h. Theophylline level in blood, and effluent were measured twice, after second and tenth hour of procedure. After 10 hours of CVVHDF the drug level decreased to 75 mg/L, and significant improvement in the patient's condition was observed. Theophylline clearance was 34 mL/min at 2, and 36 mL/min at 10 hours with drug removal rates of 306 mg/h and 162 mg/h respectively. *Conclusions:* Continuous veno-venous hemodiafiltration may be considered as a viable treatment option in chosen drug intoxications, especially in patients with hemodynamic instability. Theoretically CVVHDF seems to be more effective than charcoal hemoperfusion because of its higher clearance and the possibility of removing substances with a wide range of molecular weights and those with higher plasma protein binding affinity. *References:* 1. Okada S, Teramoto S, Matsuoka R. Recovery from theophylline toxicity by continuous hemodialysis with filtration. Ann Intern Med 2000; 133:922.

32. Comparative Evaluation of Glasgow Coma Score and Gag Reflex in Predicting Aspiration Pneumonitis in Acute Poisoning

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Objective: 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). *Methods:* In a retrospective analysis study after prospective data collection, 155 poisoned patients with GCS ≤ 12 were evaluated. An assessment of GCS and the quality of gag reflex were made on arrival and recorded. Intubation status before gastrointestinal decontamination was noted. All patients were subsequently followed for development 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). *Conclusion:* A reduced GCS and a nonintubated trachea are associated with an increased incidence of AP.

33. Survey of the Role of the Clinical Laboratory in Seventeen Frequent Overdoses

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Objective: To evaluate physicians' views on the role of laboratory tests in the management of frequently encountered overdoses. *Methods:* A 20-item questionnaire was distributed to the attendees of clinical toxicology courses directed to physicians working in emergency medicine and primary care. Ninety-five questionnaires were completed. This communication focuses on one item of this questionnaire: "Indicate the three tests that you consider fundamental for the clinical care of the following 17 frequent overdoses". *Results:* Respondents stated that the tests they found most valuable for each case were the following (Table 1). Physicians, in our setting, have the perception that the laboratory's primary role in the care of overdose patients is providing non-specific tests. When asked about overdoses caused by a substance/drug that the laboratory can quantify, respondents did not state the specific test in first place of importance in any of the poisonings. In the case of lithium, its quantification was placed in second order of frequency, whereas for paracetamol and salicylates, levels were put into third place. In poisonings involving drugs frequently abused where urine identification is available, (opiates, cocaine, benzodiazepines, amphetamines and gamma-hydroxy-butyrate) the first answer was toxicological screening except for cocaine, where troponin I was considered more valuable. *Conclusion:* One of the most interesting conclusions of this part of the survey is that after making a clinical diagnosis, physicians are more concerned with tests that reveal information about the state of target organs rather than levels of toxic substances. *References:* 1. Desel H. Need for Laboratory Investigation Support in Diagnosis and Treatment of Poisonings - Results of a EAPCCT Membership Survey (abs). Clin Toxicol 2009; 47:441–442.

Table 1. Most valuable laboratory tests

	Answer option					
	First	**%**	**Second**	**%**	**Third**	**%**
Ethanol	Glucose	35	AST/GOT	11.9	Screening	11.1
Benzodiazepines	Screening	33.9	Arterial gases	27.6	Venous gases	10.7
Antipsychotics	CPK	33.9	Arterial gases	27.6	Venous gases	10.7
Antidepressants	Screening	22.2	Ions	12.0	Arterial gases	11.1
SSRI	Screening	23.3	Venous gases	12.2	Creatinine	11.1
Paracetamol	AST/GOT	34.1	Prothrombin time	19.3	Serum levels	16.7
ASA	Venous gases	17.1	Hb/prothrombin time	11.1	Serum levels	8.8
Lithium	Creatinine	24.7	Serum levels	21.2	Ions	13.2
Cocaine	Troponin i	28.3	Screening	27.1	CPK	22.2
Heroine	Screening	43.4	Arterial gases	27.1	Glucose	8.6
GHB	Screening	29.2	Glucose	11.2	Crea/arterial gases	9.6
Methanol	Venous gases	18.6	Lactate	15.7	Arterial gases	11.4
MDMA	Screening	29.0	CPK/troponin I	13.1	Creatinine	10.0
Caustics	Haemoglobin	24.4	Arterial gases	15.1	Venous gases/WBC	8.6
Smoke	Carboxi-hb	38.2	Arterial gases	26.3	Lactate	19.1
Mushrooms	AST/GOT	19.7	Prothombin time	13.6	GGT	11.5
Pesticides	AST/GOT	14.7	Arterial gases	13.1	Creatinine	11.4

34. Molecular Identification of *Lepiota brunneoincarnata*: Application to the Clinical Setting

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Objective: Amatoxin poisoning is ascribed to 35 amatoxin containing species belonging to the genera *Amanita, Galerina* and *Lepiota*.[1] The high degree of polymorphisms within the ITS nrDNA region has been used in the identification of fungal species and separation of species, as well as to establish the limits between very closely related taxa. This is the first description of the application of the study of the regions ITS-1 and ITS-2 to the resolution of a mushroom poisoning caused by *Lepiota brunneoincarnata*. *Methods:* Mycological identification of the mushroom fragments observed in the meal was made by botanical classification with macroscopic and microscopic characteristics. ITS-1 and ITS-2 regions were studied by PCR and subsequent sequencing analysis.[2] Sequencing data were compared with homologous sequences located at public databases (Blast search, NCBI). Searching for amanitins was made by High Performance Thin-Layer Chromatography (HPTLC) applied to the cooked mushrooms. *Results:* Three patients from a family suffered from hepatotoxic poisoning after eating a stew of mushrooms. The samples were picked from a lawn in a public park in the city of Valencia. The Spanish Poison Center was contacted 18 hours after ingestion. The main complaints at this moment were vomiting, colic, abdominal pain and diarrhea. Hepatic transaminases were slightly elevated. Macroscopic examination of the mushroom fragments led to no conclusive result. Ellipsoid smooth thick-walled hyalin spores were seen in the sample. The staining of spores with Melzer´s iodine reagent turned reddish (dextrinoid reaction). Both results suggested the presence of a member of the genus *Lepiota*. The blast search of the ITS1 and ITS2 nrDNA sequences showed 99% similarity with a sequence of *Lepiota brunneoincarnata*. Alpha and beta amanitins were detected by HPTLC. *Conclusion:* Molecular methods can be used to develop diagnostic tests for fungi. Comparative analysis against GenBank database was useful in the identification of this species. *References:* 1. Roux X, Labadie P, Morand C, et al Mushroom poisoning by brunneoincarnata: about two cases. Ann Fr Anesth Reanim 2008; 27:450–2. 2. Iturralde MJ, Ballesteros S, Ramoacuten MF, et al. DNA Profiling: A promising tool for mushroom poisoning diagnosis. Clin Toxicol 2004; 42:535.

35. "CityParade": Mixed with GHB

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Objective: CityParade is an electronic music festival bringing together about 300,000 adolescents and young adults in the center of cities. It was held in 2005 and 2007 in Liege and in 2006 in Charleroi. With a strict goal of health safety, specialized toxicology analyses were made available to doctors holding advanced medical positions. Blood and urine analyses and solid and liquid analyses were carried out, for the most part, in real time, day and night. *Methods:* According to the analysis envisaged and the particular hospital involved, large analytical facilities were available. HPLC-DAD

(High-Performance Liquid Chromatography-Diode Array Detection) for "therapeutic" medications, GC-MS (Gas Chromatography-Mass Spectrometry) by liquid injection and headspace for blood analysis for marijuana, GHB and volatiles, HPLC-MS-MS for urinalysis of other sedatives. Each analysis was carried out in real time, including a semi-quantification of GHB by HPLC-MS-MS, with the exception of the definitive quantification of GHB and blood THC. The quantification limits of all of the methods allowed dosing each molecule to the minimum positive-test threshold for sedatives and to the lower therapeutic threshold for medications. *Results:* At each festival, from 100 to 200 people required medical care. 15 to 20 on average had to be transferred to intensive care units. All presented complex symptoms with a combination of coma, delirium, agitation, convulsions, anxiety/panic attacks. . . The most frequently detected sedative was GHB (60–80% of cases), in parallel with ethanol. Followed closely by derivatives of MDMA and cocaine (50%) as well as by marijuana/cannabis (30–40% of cases). Practically no opiates were detected and no abuse of therapeutic medicines, when one excludes those given in doctor's offices. In 2005, our attention was drawn to a blue liquid mixed equal parts Orange Cognac and a glass cleaner containing butoxy-4-ethanol!

36. The Availability of Toxicological Analyses Relating to the Management of the Poisoned Patient in Ireland

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Objective: To investigate the availability in Ireland of 15 quantitative laboratory analyses, specifically relating to the management of the poisoned patient. Not all hospital laboratories perform a full complement of toxicological investigations. Although there are international guidelines on toxicological analyses needed in the poisoned patient, there are no national guidelines in Ireland and the availability of specific quantitative toxicology analyses has not been previously investigated here. *Methods:* A questionnaire relating to the availability of 15 quantitative analyses (carbamazepine, carboxyhaemoglobin, digoxin, ethanol, ethylene glycol, iron, lithium, methaemoglobin, methanol, paracetamol, paraquat, phenobarbitone, salicylate, theophylline, and valproic acid) was compiled and distributed electronically to all 39 acute hospital laboratories in Ireland. Respondents were asked which quantitative analyses were available and if they were provided on-call (out-of-normal working hours). Data was collected from November 2008-February 2009 inclusive. National statistics for acute hospital emergency department (ED) attendances in 2008 were obtained. Hospitals were sorted into groups according to their number of ED attendances: (A) <20,000 (n = 9 hospitals), (B) 20,000–30,000 (n = 11), (C) 30,000–40,000 (n = 7), (D) 40,000–50,000 (n = 7), (E) >50,000 (n = 5). The median number of assays provided for each hospital group was calculated. *Results:* The response rate was 100%, allowing complete national data to be ascertained. Only 1 hospital laboratory provided the full complement of 15 toxicological assays. Three laboratories did not provide any toxicological analyses. Nationally, 15 hospital laboratories (38.5%) performed at least 10 of the 15 toxicological investigations. Paracetamol was the most widely available assay (74.4%, n = 29) and the assays with lowest availability were methanol, ethylene glycol and paraquat (2.6%, n = 1). Hospital laboratories in Group A and B carried out a median number of 3/15 assays (range 0–8) and 4/15 assays (range 0–10) respectively. Hospital laboratories where ED attendances exceeded 30,000 per annum carried out a median number of 11/15 toxicological assays (range 1–15. *Conclusion:* Toxicological investigations are widely available in acute Irish hospital laboratories and most analyses are provided on a 24-hour basis. Hospitals with ED attendances in excess of 30,000 provided a more comprehensive laboratory service with respect to quantity of analyses performed.

37. Reliability of Different Methods Useful in Emergency Services for PH Measurement of Potentially Caustic Solutions

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Objective: Precise and rapid pH determination of unknown potentially caustic solutions could be very useful in Emergency Departments (EDs). However the reliability of some methods available in EDs, such as pH paper strips, can not be always guaranteed. The aim of this study was to evaluate the reliability of different methods for pH-measurement in emergency setting. *Methods:* Four different methods for pH detection were analyzed: laboratory pH-meter, urine pH-strips 5 to 9, pH-strips 0 to 14 and pH-strips 1 to 11. Caustics tested were chosen from among those most involved either in accidental and intentional exposures in Pavia Poison Centre experience. Methods were blind tested by four operators: one chemist and three senior toxicologists. *Results:* Reliability of pH methods was evaluated on 19 products (2 peroxides, 4 hypochlorites, 3 strong acids, 8 strong alkalis and 3 alcoholic detergents). No significant differences in pH detection were registered among operators. PH-meter was able to provide the same pH data to those declared in the product SDS. PH-strips 0–14 and 1–11 are trustworthy methods for pH measurement of strong acids, strong alkalis, peroxides and alcoholic detergents. Contrarily for hypochlorites these methods provided erroneous pH measurements ranging from 5.5 to 8 instead of pH-meter real value of 11.5. Urine pH-strips showed pH 5 for strong acids (instead of pH-meter real values of 0–2) and pH 9 for strong alkalis (instead of pH-meter real values of 10–14); moreover, erroneous values (pH from 6.5 to 8) were detected for hypochlorites (pH-meter real value 11.5). *Conclusions:* At present, pH strips 0–14 and 1–11, when available in EDs, correctly detect strong acids (pH < 2), strong alkalis (pH > 10) and peroxides, but not hypochlorites. Erroneous hypochlorite pH evaluations may be due to the whitening effects of chlorine on colorimetric strips. In case of detection of a pH ranging from 2 to 10 with colorimetric strips, a further detection with a pH-meter should be performed if hypochlorites cannot be excluded.

38. False-Positive Ethylene Glycol Levels in Diabetic Ketoacidosis. Suspected Interference of 2,3-Butanediol in an Enzymatic Ethylene Glycol Assay

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Objective: A patient with diabetic ketoacidosis (DKA) presented with a high osmolar gap and anion gap acidosis during two separate hospitalizations (initial blood glucose > 699 mg/dL and 1161 mg/dL respectively. Serum ethylene glycol levels were 24 and 30 mg/dL respectively (NorDx assay, Gas Chromatography (GC) analysis). The patient denied ingestion of ethylene glycol and the positive assay was suspected to be a false positive result as has been reported for some GC and enzymatic methods. The interference of 2,3-butanediol, previously found to be an interfering substance in ethylene glycol assays in the setting of DKA, was investigated. *Methods:* The interference of 2,3-butanediol in an enzymatic ethylene glycol assay was measured using Microgenics MGC 240. The assay uses glycerol dehydrogenase and measures the rate of formation of NADH by spectrophotometry. The ethylene glycol level in the patient's serum sample was then measured. *Results:* The ethylene glycol assay using the MGC 240 method is linear between 1–100 mg/dL ethylene glycol ($R^2 = 0.998$). 2,3-Butanediol poses a positive interference in the assay in agreement with a previous report in the literature. The assay exhibited a linear response to 2,3-butanediol between 1 and 40 mg/dL ($R^2 = 0.962$). The assay is surprisingly more sensitive to 2,3-butanediol than ethylene glycol. Five and twenty mg/dL (0.56 mmol/L and 2.22 mmol/L) 2,3-butanediol caused a 66% and 427% interference to the measurement of 20 mg/dL of ethylene glycol (3.22 mmol/L) respectively. Our patient's serum ethylene glycol level was <1 mg/dL using the Microgenics assay. This confirmed the false positive result. It also indicated that 2,3-butanediol was absent in our patient's serum. *Conclusion:* We report a patient who had false-positive ethylene glycol levels in the setting of DKA. 2,3-Butanediol, previously described as an interfering substance and cause of false-positive ethylene glycol levels in the setting of DKA, was not the cause of the false positive ethylene glycol results in our patient. Other compounds in the serum of patients with DKA such as alpha-hydroxyaldehydes and beta-hydroxyketones may interfere with the GC analysis of ethylene glycol. Identification of these interfering compounds is currently underway.

39. A Classic Presentation of Chloral Hydrate Overdose: Coma and Cardiac Dysrhythmia and the Phenomenon of Myocardial Sensitization

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Objective: Chloral hydrate is one of the oldest sedative-hypnotic medications still in use. It is metabolized via alcohol dehydrogenase to an active metabolite trichlorethanol. Trichlorethanol is responsible for the hypnotic effects of chloral hydrate as well as the majority of adverse effects seen in overdose. Trichlorethanol increases myocardial sensitivity to circulating catecholamines resulting in potentially fatal dysrhythmias. Most deaths attributable to chloral hydrate are due to cardiac dysrhythmia. Electrocardiographic changes may be refractory to standard ACLS protocol. Beta blockers have been used successfully for persistent cardiac dysrhythmia. We include a classic presentation of chloral hydrate overdose and discuss the phenomenon of myocardial sensitization. The use of beta blockade and specific supportive cares in chloral hydrate overdose are also reviewed. *Case report:* A 51-year old female with a history of major depressive disorder and alcohol abuse called Emergency Medical Services reporting a suicide attempt. When the ambulance arrived she was comatose. A nasal trumpet was inserted and naloxone was administered empirically with no response. Initial vital signs en-route to the hospital included a heart rate of 130–180 beats-minute, blood pressure of 113/47 mmHg and respiratory rate of 14 breaths-per-minute. In the ambulance the patient showed a wide-complex rhythm of undeterminable origin on the cardiac monitor. In the Emergency Department (ED) she was intubated and sedated with benzodiazepines and propofol. A subsequent electrocardiogram demonstrated a primarily narrow-complex tachycardia with frequent atrial and ventricular ectopy. Magnesium sulfate, sodium bicarbonate and calcium chloride were given without change in rhythm. The family arrived with an empty bottle of chloral hydrate and in consultation with Poison Control an esmolol drip was prepared. The patient's ectopy diminished after sedatives and decreased physical stimulation however and esmolol was never administered. Trichloroethanol levels returned elevated at 108 mg/L. The patient was extubated only 12 hours after presentation and had complete resolution of her symptoms. *Conclusion:* The hallmark features of chloral hydrate overdose include coma and cardiac dysrhythmia which may be refractory to standard ACLS protocols. Cardiac dysrhythmias, primarily due to myocardial irritability and sensitivity to circulating catecholamines, may respond to beta blocking agents.

40. Coma Blisters, Pressure Injury and Quetiapine Overdose

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Objective: Skin lesions and blistering in the overdose patient are commonly referred to as coma blisters.

Historically associated with barbiturate overdose, coma blisters have also been colloquially referred to as 'barb burns'. We present a patient who suffered a prolonged coma after quetiapine overdose and was noted to have skin lesions including bullae and blistering. In comparing the mechanism of tissue injury to other types of pressure injury such as decubitus ulcers we discuss the role that pressure injury and subsequent impairment in tissue oxygenation plays versus specific drug effects such as endothelial disruption and microvascular thrombus formation in the evolution of this type of injury. *Case report:* A 27 year-old male was transferred to our tertiary care center with the history of ingesting 7200 mg of quetiapine in a suicide attempt. He had been found comatose, having ingested the quetiapine up to 35 hours prior to being discovered. He was agitated, tachycardic and febrile on arrival and complained of diffuse myalgias and weakness. The patient was noted to have multiple vesicles on his right ankle and a firm, erythematous plaque and bullae on his right thigh. Laboratory abnormalities included an elevated CK at 33,000. The patient's course was complicated by bacteremia and cellulitis, associated with ruptured bullae, of his right hip. With treatment of his infection, wound care, and hydration for rhabdomyolysis the patient improved and was ultimately discharged to self-care. *Conclusion:* Sequelae related to prolonged immobility of any cause may include injury to muscle, vascular, microvascular and cutaneous structures. Coma blisters differ from pressure ulcers in many ways and cannot be graded using the typical staging system; injury may extend beyond intact cutaneous structures to accompanying deep tissue including muscle, nerve and vascular structures. The degree of injury is often under appreciated and may lead to complications including compartment syndrome, neuropathy, bacterial infection and wounds resembling severe burns. Histopathologic analysis suggests an array of microvascular injuries which are secondary to direct pressure injury, as well as specific drug effect. Appropriate attention to coma blisters and related injuries will decrease morbidity and mortality related to drug overdose.

41. Remarkable Dissociation Between Phenobarbital Serum Levels And Clinical Presentation in a Suicidal Attempt

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Objective: To report a clinical case where very high serum levels of phenobarbital did not lead to the expected neurological effects. *Case report:* A 38 year old lady was brought to the ER with a history of having ingested 20 phenobarbital (100 mg each) pills 45 minutes earlier together with 70 mg of metoclopramide in a suicidal attempt. At admission she presented sleepy with SpO_2 of 80%. Gastric lavage was then performed, and nasal oxygen and 1 mg/kg activated charcoal were administered. Due to epileptic syndrome she had been using 200 mg phenobarbital per day regularly for the last 5 years. Patient improved SpO_2 during the first hours of observation and remained a little sleepy but conscious after 24 hours observation when phenobarbital serum dosage was performed by immunoassay technique showing 136.45 mcg/mL (confirmed by LC/MS = 140.15 mcg/mL). ICU team was advised performing urine alkalinization, although urine pH never reached 7.5. The patient remained sleepy during the whole hospital period. Four more blood samples were withdrawn aiming to measure phenobarbital and show levels compatible with an indication for haemodialysis, until 112 hours after the ingestion (58.8 mcg/mL). Results are shown in Table 1. Haemodialysis was not performed. *Conclusion:* Tolerance to phenobarbital CNS toxic effects is well known among chronic regular users,[1] although such high levels have never been seen so far, and for so long a period of time, without any major CNS depression. *References:* 1. Butler TC, Mahaffee C, Waddell WJ. Phenobarbital: studies of elimination, accumulation, tolerance, and dosage schedules. J Pharmacol Exp Ther 1954; 111:425–35.

Table 1. Serum levels of phenobarbital by two methods

Time after ingestion (hours)	Immunoassay (μg/mL)	LC/MS* (μg/mL)
24	136.45	140.15
44	109.05	112.62
78	81.34	64.26
96	86.18	59.8
112	–	58.8

*Liquid chromatography/mass spectrometry

42. Intra-Arterial Infusions in the Treatment of Skin Exposures to Hydrofluoric Acid

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Objective: Hydrofluoric acid is often confused with hydrochloric (muriatic) acid but exhibits different local and systemic effects, and a high index of suspicion for fluoride exposure is important in burn cases. Treatment of burns from hydrofluoric acid is still problematic. *Case report:* A 24-year-old worker was exposed at work to a brick-cleaning solution. Despite immediate and copious rinsing of his affected dominant hand (the right hand), pain developed within four to five minutes of exposure and persisted throughout the rest of the day and the night. The patient, his wife, and a co-worker reading the label of the cleaning solution all reported that the cleaner was muriatic acid (hydrochloric acid), but further investigation established that it was in fact hydrofluoric acid. Local pain was unresponsive to topically applied calcium-gluconate gel, and an interscalene block was performed on the right brachial plexus, an arterial line was placed into the right radial artery, and calcium gluconate was administered both intra-arterially (using a four-hour infusion) and via injection through the skin into the affected tissues. After the nerve block had worn off, the pain in the patient's right hand returned and increased, and a new four-hour intra-arterial infusion was begun. However, adequate flow into the artery was not maintained, and the infusion had to be terminated. The patient did not exhibit systemic effects from fluoride, was free of pain the following day, and was discharged. *Conclusion:* Intra-arterial therapy for hydrogen-fluoride exposures has both promise and also problems, and an appreciation of both is necessary before deciding upon this route of administration. *References:* 1. Lin TM, Tsai CC, Lin SD, et al. Continuous intraarterial infusion therapy in hydrofluoric acid burns. J Occup Environ Med 2000; 42:892–7.

43. Beneficial Effects of 'Home Therapies' on the Pharmacokinetics of Paracetamol poisoning - a Human Simulated Overdose Study

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Objective: To assess whether raw eggs or a fluid bolus, given orally ten minutes after paracetamol ingestion, affect the rate and degree of paracetamol absorption. *Methods:* The study was an open, cross-over, randomized human simulated overdose study, including 15 healthy adult male and female volunteers. Paracetamol was used as a marker for gastric emptying time. Formulated as immediate disintegrating and release tablets, paracetamol 50 mg/kg bodyweight was dosed on three occasions. On the control day only paracetamol was ingested. On two intervention days each volunteer received two raw eggs (whole, homogenised) or 150 mL of water on one occasion each. Pharmacokinetic parameters (T_{max}, $AUC_{0-\infty}$, C_{max} and elimination half-life) for the marker paracetamol were calculated from serum-paracetamol concentrations collected at 19 separate time points. *Results:* A summary of the pharmacokinetic parameters is included in Table 1. *Conclusion:* Raw eggs significantly slowed gastric emptying and lowered maximum serum-paracetamol concentration compared to non-nutrient containing water and to control where no intervention was performed. The total body drug load was not significantly affected by the egg ingestion. These results should impact the treatment of immediate poisoned patients. In cases where a highly poisonous xenobiotic has been ingested, subsequent ingestion of raw eggs may slow down the emergence of toxic symptoms and allow timely treatment, thus increasing chances of survival.

44. *Status Epilepticus* Secondary to Diphenhydramine Overdose

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Objective: Diphenhydramine (DPH) is an H1 histamine antagonist that is commonly used for allergic reactions, colds and cough, and as a sleep aid. In addition to anticholinergic and antihistaminergic effects, sodium channel blockade becomes evident following DPH overdose. While seizures may occur following overdose of DPH, status epilepticus (SE) is distinctly uncommon. We report a case of SE and wide-complex dysrhythmias following an intentional overdose of diphenhydramine. *Case report:* A 36 year-old woman with a past medical history of hypothyroidism on levothyroxine was brought to the emergency department (ED) in SE by emergency medical services (EMS). One hour after an argument with her husband he found her lethargic in a locked room. Initial vital signs were: blood pressure, 80/55 mmHg; heart rate, 160 beats/minute; respiratory rate, 20 breaths/minute room air oxygen saturation, 99%; capillary glucose, 7.2 mmol/L. The generalized seizures continued for duration of 35 minutes, despite the administration of 8 mg of intravenous lorazepam. The patient underwent endotracheal intubation and a propofol infusion was initiated which terminated her seizures. An electrocardiogram revealed a wide-complex tachycardia with QRS duration of 120 msec, which responded to 220 mEq of intravenous sodium bicarbonate. The patient was in the intensive care unit for two days and neurologically intact upon extubation. An empty bottle of DPH was brought in by the husband and her serum DPH concentration was reported as 1200 ng/mL; a

Table 1. Primary and secondary endpoints. Values are calculates as mean (N = 15), [range]

Study Day	T_{max} (min)	$AUC_{0-\infty}$ (min*umol/L)	C_{max} (umol/L)	Elimination half-life (min)
Control	64 [31–346]	74054 [52950–119655]	279 [134–435]	153 [105–201]
Water	93 [31–182]	74245 [54913–150627]	283 [147–381]	150 [110–286]
Egg	180 #,$ [51–245]	71653 [39126–111119]	189 #,$ [121–322]	144 [99–294]

#Significant difference compared to control, $P < 0.05$
$Significant difference compared to water, $P < 0.05$

tricyclic screen was negative. While seizures and sodium channel blockade are recognized complications of DPH toxicity,[1] we were unable to find reported cases of SE from diphenhydramine overdose. Elements of the patient's presentation were similar to a tricyclic overdose and management required aggressive control of her seizures, sodium bicarbonate therapy, and recognizing that physostigmine was contraindicated due to wide complex tachycardia. *Conclusion:* A patient with a DPH overdose may present with SE. Management should focus on antidotal therapy with sodium bicarbonate, consideration of physostigmine, and supportive neurological management with appropriate anticonvulsants and airway protection if clinically indicated. *Reference:* 1. Sharma AN, Hexdall AH, Chang EK, et al. Diphenhydramine-induced wide complex dysrhythmia responds to treatment with sodium bicarbonate. Am J Emerg Med 2003; 21:212–215.

45. Emergency Department Management of Unintentional Pediatric Ingestions of Psychiatric Medications

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Introduction: Pediatric toxic ingestions though rare, can be life-threatening. Little data is available regarding treatment and outcomes of a pediatric patient who unintentionally ingests psychiatric medications. *Objective:* To determine the emergency department (ED) course of pediatric patients who unintentionally ingest psychiatric medications. *Methods:* Design: A multi-center retrospective cohort. Setting: 20 New Jersey and New York EDs in urban, suburban and rural areas from January 2007 to September 2009. Subjects: Consecutive patients 0–8 years of age with the ICD-9 primary diagnosis of "poisoning antidepressants." A manual chart review was performed for specific data points. This study was approved by the hospital Institutional Review Board (IRB). *Results:* The database contained 44 patients age 0–8 years with an ICD9 diagnosis of "poisoning antidepressant." Charts were available for 38. Eleven were excluded for non-psychiatric medication ingestions, leaving 27 for evaluation. Ten patients were admitted, two transferred and the remaining discharged. Median age was 2.6 years. Males comprised 55% (n = 15). Poison control was contacted in eighty-one percent. The most common classes of medications were: SSRI (n = 13), antidepressant unspecified (N = 5), SNRI (N = 4), antipsychotic (N = 3), and TCA (N = 3). Admission rates based on class of medications were: 53%, 40%, 0%, 33%, and 66%, respectively. Fifteen were ultimately discharged from the ED. Lethargy was documented in 4 patients (antipsychotic n = 3/3, antidepressant n = 1/5) of which 50% were admitted. EKGs were documented in 70% of patients and 47% additionally recorded QTc - all were normal. One patient had a documented cardiac arrhythmia, bradycardia (antidepressant) which occurred prior to ED arrival. Six patients received charcoal and 2 had gastric lavage performed, of which one was discharged. No charts recorded patient decompensated while in the ED. No "bounce back" visits occurred for any discharged patients to participating hospitals. *Conclusion:* In our study, it was rare for pediatric patients, who unintentionally ingest psychiatric medications, to have cardiac abnormalities and none decompensated while in the ED.

46. Are Pediatric Patients who are Severely Afflicted by Carbon Monoxide Poisoning Receiving Hyperbaric Oxygen Therapy?

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Introduction: Carbon monoxide (CO) can lead to devastating end organ effects. Limited data is available regarding pediatric patients presenting to the ED with "severe" CO exposure and the utility of hyperbaric oxygen therapy (HBO). *Objective:* To determine if the sickest pediatric patients exposed to CO receive HBO. *Methods:* Design: Multi-center retrospective cohort study. Setting: 23 NJ/NY EDs. Subjects: Consecutive patients (ages 0–21 yrs) with the ICD-9 diagnosis of "toxic effects CO" from Jan 2000 to Oct 2006. A manual chart review was performed. We "*a priori*" defined "severe" intoxication as: syncope, altered mental status, dizziness, seizures, cardiac arrest or a CO level (COhgb) >20%. Statistics: Mann-Whitney with preset alpha of 0.05. *Results:* "Toxic effects of CO" was diagnosed in 380 pediatric patients. 362 charts were available for analysis, 49 (13.5%) met inclusion criteria as "severe," and 40 had documented COhgb levels with a mean of 11.2% (95% CI 8.2–13.2). Mean CO levels of those treated with HBO was 23.5% (95% CI 18.5–28.5) (p = <0.009). HBO was utilized in 14% (N = 7) of patients - (one with a CO level < 20). Median age was 13.8 and 17 years overall and in HBO groups, respectively. Four patients required transfer for treatment. Norm baric O_2 was utilized in 75%. The most common source of exposure (43%) was home CO alarm triggered. Eighty-six percent (N = 42) of patients were ultimately discharged. *Conclusion:* Treatment of the sickest CO intoxicated pediatric patients is variable with only a minority receiving HBO.

47. The Tell-Tale Heart

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Objective: To describe an uncommon side effect of quetiapine abuse in a 45 year old woman who consumed 13 tablets of quetiapine for suicidal purpose. *Case report:* A 45 year old woman, guest of a private clinic, was brought to our ED after taking, about an hour before, 13 tablets of quetiapine 100 mg. On arrival, the patient was quiet, alert and cooperative, GCS was 14, the heart activity was rhythmic, no chest pain was described. Vital parameters were normal, TA 160/90, FC 102, T 36.5 °C, sats 96%. Two venous accesses were obtained, beginning hydration. The first ECG, performed 5 minutes after the arrival, was normal. Fifteen minutes later the patient complained of retrosternal pain with mild dyspnea. A second ECG showed a three millimeter ST elevation in I and II. A $NaHCO_3$ infusion was established (150 mEq in 30 minutes + continuing infusion) until a plasma pH of 7.50 was reached, with a rapid improvement of clinical condition and ECG normalization 90 minutes later. The patient was subjected to gastric lavage and plasma alkalosis was maintained for 12 hours without signs of cardio- or neurotoxicity during clinical observation. She was released 18 hours after arrival and transferred back into the private clinic. *Conclusion:* Common side effects of quetiapine include weight gain, constipation, headache and dry mouth. Six to seven percent of patients may experience tachycardia. Less common side effects (less than 1% of patients) include abnormal liver tests, dizziness, upset stomach, substantial weight gain, a stuffy nose, akathisia and increased paranoia. ECG abnormalities are very uncommon. In this case we want to point out how these changes were completely normalized without the use of cardiac-specific drugs, but only with sodium bicarbonate infusion.

48. 'Scrotocaine': Toxicity from Scrotal Infusion of Lidocaine

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Background: Intentional distension of the scrotum is a discrete yet well described form of autoeroticism. Reported complications have predominantly infectious etiologies. We describe a case of acute lidocaine poisoning secondary to scrotal infusion. *Case report:* A 50 year-old man presented to the emergency department (ED) with confusion after a near-syncopal event. Two hours prior to arrival he had injected 80 mL of undiluted 2% viscous lidocaine (16 mg/kg) into his scrotum, and nearly immediately developed palpitations and lightheadedness. The patient reported that he regularly and safely performed such infusions with aqueous lidocaine in attempts to reduce the discomfort associated with the subsequent scrotal infusions of up to one liter of sterile saline. Vital signs were normal. He was somnolent and disoriented, but gradually improved during the first hour, and later recalled feeling "drunk". As his mental status improved his BP increased from normal to his mildly hypertensive baseline. Examination noted mild generalized cyanosis and an enlarged scrotum (diameter ~20 cm) with multiple punctuate scars on the scrotum and glans penis. ECG revealed sinus rhythm, normal intervals, LVH without ectopy, and inferior T-wave inversions that were unchanged from baseline. Serum electrolytes were normal and ethanol was undetectable. Serum lidocaine concentrations were 5.6 mcg/mL at 2 hours post-infusion and 0.54 mcg/mL at 7 hours (antidysrhythmic range: 2–5 mcg/mL). He was admitted to telemetry for one day without symptoms or ECG events, signed out against medical advice, and declined recommendations to abstain from scrotal infusion. *Discussion:* Scrotal 'inflation', as it is known in the lay literature, while not a mainstream form of autoeroticism, is detailed by several websites. Its popularity may be facilitated by the commercial availability of sterile medical supplies. To lessen the discomfort of large-volume infusions some enthusiasts reportedly advocate pretreatment with local anesthetics, often available from the same websites which have not cautioned against medication complications. Altered sensorium, seizures, and cardiac arrest may manifest when serum concentrations approach those demonstrated by this patient. Supportive care generally suffices although there is one reported fatality from genital subcutaneous injection of bupivicaine. *Conclusion:* Scrotal infusion of lidocaine and other local anesthetics may result in neuro-cardiovascular toxicity. Practitioners should be notified of the risks.

49. 'Popper' Retinopathy: Acute Isobutyl Nitrite Exposure Induces Red to Yellow Color Visual Disturbance

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Objective: Only two reviews list "yellow vision" resulting from volatile alkyl nitrites, both of which incorrectly cite a century-old textbook that described inconsistent subjective color vision changes in patients inhaling amyl nitrite. We report a case of acute red to yellow color perception that lasted over one month following isobutyl nitrite use. *Case report:* A 26 year-old man reported that for two days red light sources appeared yellow with halos following use of isobutyl nitrite. He could still distinguish red and yellow pigments. He denied medications or other abused substances, and noted mildly decreased visual acuity in his right eye at baseline, but denied other medical history. Vital signs were normal. Uncorrected visual acuity was 6/15 OD and 6/8 OS. Intraocular pressures were 14 mmHg OU. Pupils were equal, round, and reactive to light and accommodation. Extraocular movements were full and symmetric. He passed standard monocular color vision testing. Indirect funduscopy revealed abnormal yellow deposits with mottled retinal pigment epithelium more apparent on the right fovea, and an intraretinal splinter hemorrhage along the right inferior arcade. Fluorescein angiography demonstrated a hyperfluorescent pattern in the inferior right fovea, perhaps representing dilated vasculature. Optical coherence tomography revealed hyperreflectivity at the level of the

inner segment/outer segment junction of the photoreceptor layer of both eyes. Unfortunately he did not return for electroretinography or follow-up with a retinal specialist. However, he reported via telephone that his symptoms gradually resolved over 6 weeks. It is unlikely that the change in color perception is due to selective ischemia/infarction of long wavelength photoreceptor cells. A more appropriate explanation is that volatile nitrites affect a specific susceptible target in long wavelength photoreceptor cells or their downstream cells. It is possible that as nitric oxide donors, alkyl nitrites disrupt ATP production in these metabolically sensitive cells or activate G-proteins which may induce color misperceptions via activation of cone cGMP-gated sodium channels in a mechanism analogous to that proposed for phosphodiesterase inhibitors. *Conclusion:* Volatile alkyl nitrites can induce red to yellow color visual disturbances that may persist beyond the duration of cardiovascular and hematologic effects.

50. A Case of Life-threatening Rectal Administration of Moist Snuff (Snus)

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Introduction: Oral use of moist snuff ("snus"[swe]) is common among young males in Sweden, especially among extramural athletes. At least 23% of Swedish men use moist snuff on a regular basis. In excessive doses, nicotine may cause agitation and in rare cases unconsciousness. However, nicotine uptake is higher in an alkaline medium and thus rectal administration is probably more efficient than buccal administration, due to the higher rectal pH. We here describe a case of nicotine poisoning via excessive rectal self-administration of moist snuff in an attempt to treat a migraine attack. *Case report:* A previously healthy, 42 year-old man, arrived at the emergency ward of a local county hospital with symptoms of nausea, discomfort and dizziness. The patient had suffered a severe migraine attack and intended to treat himself as usual with rectal administration of snus. Due to lack of response, about 75 sachets (sic!) of snus were administered. He presented to hospital with dry and warm skin, a pulse rate at 53 b/min and mean arterial blood pressure (MAP) at 135 mm Hg. On arrival at the emergency department the patient had fluctuating consciousness, Glasgow Coma Scale (GCS) at 7–8 and he was increasingly agitated and confused. The condition gradually worsened and the patient became comatose with anisocoria. The patient was treated symptomatically. No specific anti-nicotinergic treatment was given. Plasma levels of the nicotine metabolite cotinine were 8691 µg/L seven hours after admission and even higher after twelve hours at 9814 µg/L. All physiological functions were completely restored within 24 hours and he was discharged from hospital after 36 hours. *Conclusion:* Excessive rectal administration of moist snuff may lead to a life-threatening condition. Severe cases, such as this should be monitored in an intensive care unit with invasive monitoring of blood pressure and possibilities to intervene quickly when needed. Public information on the harm of excessive administration of snus seems to be needed.

51. Anesthetic Veterinary Drug Poisoning After Ingestion of Deer Venison

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Objective: Wild deer breeding is used for reintroduction in protected areas like natural parks and private estates. The capture of animals is carried out using a dart syringe with an anesthetic drug shot with a rifle. Tiletamine in association with zolazepam are used in veterinary medicine for that purpose. Tiletamine is a NMDA antagonist with dissociative anesthetic effects similar to ketamine while zolazepam is a pyrazolodiazepinone structurally related to benzodiazepine. We here describe the first known case of veterinary drug intoxication after ingestion of deer venison with laboratory proof. *Case report:* A family of three, father (a forest service officer), mother and their 17-year-old son cooked and ate for lunch the last three pieces of frozen deer venison they had received after a selective hunting. That venison had been eaten before without any problems. After 15 minutes all the patients showed dizziness and nausea. While the adults recovered rapidly, the boy showed somnolence, slurred speech, alteration of thinking, confusion, visual hallucinations (blood on the bed) and amnesia. He arrived at our hospital late in the evening when most of the symptoms were resolved. Nystagmus was the only evident sign, while the vital signs and laboratory analysis were normal. Toxicology analysis for carbon monoxide, drugs of abuse, benzodiazepines and barbiturates screening were all negative. On suspicion of meat contamination with drugs, gas chromatography-mass spectrometry analysis was performed on the patient's blood and urine specimens and on the few remaining pieces of venison. Tiletamine metabolite and zolazepam were found in the patient's urine. Zolazepam serum level was 20 ng/mL; no measurable tiletamine. In the venison tiletamine concentration was 5 mg/kg and zolazepam was 2 mg/kg. The following day the boy was discharged in good condition. *Conclusion:* Human poisoning with veterinary pharmaceuticals after food ingestion has never been described before. Patients may present unusual clinical effects and may require extensive toxicological analysis for confirming the suspected exposure. The deer was probably killed or died during the capture immediately after the anesthetic shot and it was dressed instead of being discarded and the boy has eaten the piece of meat into which the dart syringe had been fired.

52. Cocaine Induced Angioedema without Urticaria: A Rare Adverse Reaction of Inhaled Cocaine

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Objective: Uvular angioedema (associated or not with IgE-mediated mast cells degranulation) is a rare disorder which may be fatal when it results in complete upper airway obstruction. We report a case of acute uvular angioedema secondary to cocaine use, poorly responsive to conventional drug treatment. *Case report:* A 32-year-old man presented to the emergency department (ED) complaining of dysphagia, muffled voice and dyspnea, 30 minutes after cocaine sniffing. He admitted cocaine use at least 2–3 times a month for several years; a similar but milder episode of angioedema had occurred one year before. He was taking no medication and had no known drug or food allergy. A diagnosis of uvular angioedema caused by cocaine or its contaminating agents was made. Aerosolized adrenaline 1 mg in association with beclomethasone 1600 micrograms was administered, followed by methylprednisolone 80 mg intravenously (iv). As the patient's condition did not improve, hydrocortisone 500 mg iv and chlorpheniramine 10 mg iv were administered, again with no evident benefit. Laboratory tests showed neutrophil leukocytosis (WBC 14210 cells/mm^3, 80.7% neutrophils) without increase of C-reactive protein values. C1 esterase inhibitor levels were 26 mg/dL (normal values 13–35 mg/dL). Urine was positive for cocaine metabolites, but no other drugs or common adulterants of cocaine (caffeine, aspirin, local anesthetics) were found. Laryngoscope examination confirmed the uvular angioedema. Symptoms resolved spontaneously 10 hours after ED presentation. *Conclusion:* Uvular angioedema has been reported after cocaine use very rarely. It may be due to thermal irritation, direct toxicity from cocaine or by type I hypersensitivity reaction to cocaine.[1,2] Cocaine-induced angioedema is likely to be more common than suspected, since there are patients with mild symptoms that do not present to the ED, as happened the first time in our patient. We suggest that clinicians should be alerted to the possibility of this unusual toxic effect of cocaine. *References:* 1. Welling A. Enlarged uvula (Quincke's oedema) - a side effect of inhaled cocaine - a case study and review of the literature. Int Emerg Nurs 2008; 16:207–10. 2. Kinsey CM, Howell M. A 27-year-old woman with a swollen uvula, chest pain, and elevated creatinine phosphokinase levels. Chest 2008; 133:809–11.

53. Levamisole-Adulterated Cocaine in A Guatemalan Body Packer

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Objective: Body packing (i.e. the internal concealment of illicit drugs for transportation) is a complex medical and ethical problem. Recently levamisole, an antihelminthic used for colon cancer or in veterinary medicine, has been recognized as an adulterant of cocaine. It is unknown if levamisole is added during cocaine processing, by distributors in the U.S., or by local dealers. Here we present a case of a body packer who developed severe cocaine toxicity from levamisole-adulterated cocaine after travelling from Guatemala. *Case report:* A 25 year old male presented complaining of abdominal pain two days after flying from Guatemala. His vital signs were temperature 97.5 °F, heart rate 125 beats per minute (bpm), blood pressure 142/82 mmHg, respiratory rate 28 breaths per minute, and pulse oximetry of 100%. An abdominal radiograph demonstrated foreign bodies within the colon. Shortly thereafter the patient had a generalized seizure. In the operating room an exploratory laparotomy was performed and twenty-one packets of cocaine were removed, including four packets with obvious breaches of the packaging. A urine gas-chromatography-mass spectroscopy (GC/MS) comprehensive toxicology screen was positive for cocaine, cocaine metabolites, and levamisole. *Conclusion:* Adulterants have been added to cocaine and other illicit drugs for many years. Recently, levamisole has been found in cocaine seized in the U.S., as well as in some cocaine users. Why is levamisole used in cocaine? Because levamisole is a white powder, it may be used to dilute the active ingredient and thus improve profits. Another theory is that levamisole improves cocaine effects by increasing dopamine and endogenous opiate concentrations. Levamisole is known to cause agranulocytosis in patients treated for rheumatoid arthritis and colon cancer. Recently physicians have recognized agranulocytosis in patients who used levamisole-adulterated cocaine. If levamisole is suspected, prompt testing of urine or plasma by GC/MS is required, as the half-life of levamisole is less than 6 hours. Our case demonstrates that levamisole is added at the source of cocaine processing. Complications arising from levamisole-adulterated cocaine are therefore expected to be widespread and not isolated to local areas.

54. Acute Respiratory Distress Associated with Inhaled Hydrocarbon

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Objective: To describe acute pulmonary toxicity from inhalation of a hydrocarbon aerosol. *Case report:* A 45 year old male presented with respiratory distress after a 15 minute inhalational exposure to Meguiar's Marine Canvas Protectant Aerosol (ingredients: liquefied petroleum gas, ethylene glycol monobutyl ether, isopropyl alcohol) in an enclosed environment. Symptoms of dyspnea, vomiting, diarrhea, near-syncope, chest tightness, and shaking chills began during the two hours following exposure. On arrival to the Emergency Department his exam was significant for heart rate 140 bpm, blood pressure 116/60 mmHg, respiratory rate 30 bpm, oxygen saturation 86% on room air, clear lungs with decreased breath sounds, and tachycardia. Initial chest x-ray showed no infiltrate but within 12 hours there was evidence of a left lower lobe infiltrate

and atelectasis. Patient's symptoms resolved with 4 liters of oxygen via nasal cannula, nebulized albuterol and 6 days of oral prednisone. No follow up data is available. *Conclusions:* Pneumonitis is a well-known complication following aspiration of ingested hydrocarbons; there is little data about pulmonary toxicity from hydrocarbon or glycol ether aerosol inhalation. Prior case reports involve products containing a fluoropolymer in combination with hydrocarbons.[1–3] Murine studies and one human case report describe subacute respiratory distress after exposure to inhaled hydrocarbons for five to seven days.[4,5] Our case demonstrates that acute pulmonary injury can occur after a short exposure to an inhaled hydrocarbon and that symptoms appear to respond to supportive measures, including oxygen, corticosteroids and bronchodilators. *References:* 1. Laliberta M, Sanfacon G, Blais R. Acute pulmonary toxicity linked to use of a leather protector. Annals Emerg Med 1995; 26:841–4. 2. Daubert GP, Spiller HA, Crouch BI, et al. Pulmonary toxicity following exposure to waterproofing grout sealer. J Med Toxicol 2009; 5:125–9. 3. Jinn Y, Akisuki N, Ohkouchi M, et al. Acute lung injury after inhalation of water-proofing spray while smoking a cigarette. Respiration 1998; 65:486–8. 4. Robledo RF, Witten ML. Acute pulmonary response to inhaled JP-8 jet fuel aerosol in mice. Inhal Toxicol 1998; 10:531–53. 5. Perrone H, Passero MA. Hydrocarbon aerosol pneumonitis in an adult. Arch Intern Med 1983; 143:1607–8.

55. Compartment Syndrome After Illicit Cosmetic Injection of Silicone Containing Lubricant

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Background: Silicone was historically used by dermatologists and plastic surgeons for cosmetic enhancement. We report a case of compartment syndrome and osteonecrosis secondary to non-medical grade silicone injections for self body enhancement. *Case report:* A 29 year old, obese man with podophilia, injected the base of his toes and thumbs with a silicone-containing personal lubricant. He presented to the hospital twelve hours later with severe pain and swelling that worsened over the next 12 hours. At that time, his right thumb had prolonged capillary refill and diminished 2-point discrimination. His toes developed blistering, weeping, and erythema on both the dorsal and volar aspects. Capillary refill was normal in the toes. The right great toe had an area of dermal necrosis extending over the volar aspect of the metatarsal. Due to signs and symptoms concerning for compartment syndrome, especially of the right thumb, the patient underwent surgical decompression and debridement of thumbs, distal feet, and toes. Intraoperatively, silicone was evacuated and necrotic fat was debrided. He never developed systemic manifestations of silicone toxicity. The patient was discharged on hospital day four. In the following four months, he underwent repeat debridement of his thumbs and toes. Ultimately, he underwent distal amputation of his right thumb for osteonecrosis. This case demonstrates a severe local foreign body reaction to non-medical grade silicone. *Conclusion:* Foreign body reactions and compartment syndrome can develop secondary to illicit cosmetic silicone injection that may require debridement similar to high pressure injection injuries.

56. Acute Strychnine-Belladonna Toxicity After Ingestion of Antique Pills Obtained from the Internet

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Objective: We present a severely ill patient who intentionally ingested pills containing strychnine and belladonna obtained from the Internet, initially interpreted as cardio-pulmonary compromise. *Case report:* A 29 year old man called an ambulance for acute onset of severe chest pain and tightness, and shortness of breath. He was alert, oriented, agitated, intermittently hallucinating, and clutched his chest in distress. Vital signs: BP 158/76 mmHg; pulse 148 beats/min; Temp 37.3°C; RR 20/min; SpO_2 100% on room air. Physical examination demonstrated diffuse repetitive myoclonus in all extremities, visually apparent involuntary contraction of chest and abdominal muscles, tachycardia, mydriasis, dry flushed skin, and clear lungs. An electrocardiogram revealed sinus tachycardia at 142 beats/minute, and a chest X-ray was normal. The tachycardia and severe chest pain prompted ordering of a CT scan, to exclude aortic dissection or a pulmonary embolism. Psychomotor agitation persisted despite escalating doses of lorazepam, and endotracheal intubation was performed. Prior to intubation he admitted to ingestion of pills containing strychnine two hours prior to presentation, but he thought there would no effect because the pills were more than 75 years old. The poison center was contacted and supportive care with aggressive benzodiazepine administration was recommended to control myoclonus. Approximately 14 hours after admission his muscular symptoms resolved and vital signs normalized allowing extubation. His family later brought in a large collection of antique pill bottles of the patient obtained from Internet purchases. Among them was an empty bottle of strychnine, belladonna, and aloin. A serum strychnine concentration, sent on arrival was 23 mcg/mL, confirming a significant exposure.[1] *Conclusion:* This patient experienced severe muscle spasms and antimuscarinic findings due to an intentional overdose of pills containing strychnine and belladonna purchased from the Internet that was initially thought to be caused by cardio-pulmonary pathology. The Internet serves as a continuing source of antiquated toxins that are sometimes forgotten and commonly thought to be only of historical interest. Strychnine should remain in the differential diagnosis of patients presenting with convulsions and preserved mental status. *References:* 1. Wood D, Webster E, Martinez D, et al. Case report: Survival after deliberate strychnine self-poisoning, with toxicokinetic data. Crit Care 2002; 6:456–9.

57. Evaluation of Altered Mental Status Due to Drug Poisoning in Iranian Adults

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Objective: Despite the existence of standard protocols for management of patients with drug poisoning resulting in a low level of consciousness, and because of varying prevalences of drugs in different countries and also the synthesis of new drugs,[1] it seems that correction of these protocols according to drug use pattern in each country and for each time course is inevitable. Our aim is to assess the characteristics of patients with drug poisoning resulting in decreased level of consciousness. *Methods:* In this descriptive cross sectional study 89 patients suffering from decreased level of consciousness due to unknown drug poisoning who were transferred to the Loghman Poison Hospital via the Tehran emergency system in March and April 2008 were consecutively selected. Demographic and poisoning characteristics, past medical history, past drug use history and level of consciousness following primary emergency care were recorded. *Results:* Seventy (79%) patients were male. The most frequent age range of patients was 20–29 years (35 patients, 39%). Thirty-three (37%) patients had a history of psychological disorders and 48 (54%) patients had substance abuse history. Decreased level of consciousness in 30 (34%) patients was due to poisoning with illicit drugs. Fifty-eight 58 (65%) patients had intentional poisoning. In intentional cases tramadol (26%) and methadone tablets (16%) were the commonest causes and in unintentional ones, Iranian kerack (29%) and opium (23%) were the commonest. Homes (53%) and parks (14%) were the most frequent target places of emergency runs. Following primary emergency care with glucose and naloxone administration in place, 31 (35%) patients remained unconsciousness. Endotracheal intubation was performed for 12 (15%) patients in place and 15 (17%) patients were transferred to ICU upon arrival to the hospital. *Conclusion:* The prominent role of opioid and illicit drugs in patients with decreased level of consciousness due to drug poisoning with about one third of these patients not recovering conscious level shows that serial studies for new drugs and correction of treatment protocols are necessary. *References:* 1. Olfson M. Gameroff M.J. Marcus S.C. et al. Emergency treatment of young people following deliberate self-harm. Arch Gen Psychiatry. 2005; 62:1122–1128.

58. An Unusual Case of Serotonin Toxicity

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Objective: Many ingested substances can cause serotonin toxicity, but antihistamines have so far not been associated with this condition. We report a case of serotonin toxicity after a massive overdose of antihistamines. *Case report:* A 22-year-old physical trainer was found unresponsive with empty bottles of a sleep medication (containing doxylamine or diphenhydramine) and of acetaminophen and with an odor of alcohol on her breath. She was transported to a local emergency department, admitted to an intensive-care unit, and noted to be profoundly somnolent, tachycardic (heart rate over 130 beats per minute), and mydriatic (pupils 5 mm OU) and to have dry skin and mucous membranes and decreased bowel sounds. Serum ethanol was 116 mg/dL. Urine drug screening was positive only for tricyclic antidepressants. Her first two acetaminophen levels were 255.5 and 210.5 mg/dL; and intravenous N-acetylcysteine was begun. In the intensive-care unit, the patient also exhibited six- to seven-beat bilateral inducible ankle clonus along with hypertonia, hyperpyrexia (38.3 °C), and pronounced lower-extremity hyperreflexia. Over the next several days, she regained consciousness and denied recent drug ingestions other than ethanol, the antihistamine sleep medication, and acetaminophen. Her temperature returned to normal and her physical examination also became normal, but her aspartate transaminase rose to nearly 2,500 U/L, and she was transferred to a different hospital for a possible liver transplant. *Conclusion:* This patient fulfilled the Hunter Serotonin Toxicity Criteria for serotonin toxicity. The cause of her increased serotonin is likely to have been her massive overdose of doxylamine or diphenhydramine, which was also probably responsible for false-positive tricyclic antidepressants on urine drug screening. To our knowledge, this is the first report of serotonin toxicity associated with large doses of an antihistamine in the absence of other serotonin-elevating substances. *References:* 1. Isbister GK, Buckley NA. The pathophysiology of serotonin toxicity in animals and humans. Clin Neuropharmacol 2005; 28:205–14. 2. Evans CE, Sebastian J. Serotonin syndrome. Emerg Med J 2007; 24:e20. 3. Fischer HS, Zernig, Schatz DS, et al. MDMA ('ecstasy') enhances basal acetylcholine release on brain slices of the rat striatum. Eur J Neurosci 2001; 12:1385–90.

59. N-Acetylcysteine and Deferoxamine as an Antidotal Therapy in a Gastrectomized Patient with Iron Poisoning

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Objective: Iron poisoning leads to systemic organ damage, being potentially lethal. We describe an iron intoxication in a gastrectomized patient and the use of N-acetylcysteine and deferoxamine as a successful antidotal therapy. *Case report:* A 48 year old gastrectomized woman was admitted to the hospital two hours after voluntary ingestion of 40 iron sulfate tablets (525 mg). On admission the patient showed no clinical evidence of iron poisoning. Gastric and whole bowel irrigation were

quickly performed. Laboratory findings showed normal values. Metabolic acidosis and hypokalemia quickly appeared and were rapidly treated. Seven hours after the ingestion, the patient presented heartburn, rectal bleeding, hypotension and tachycardia. Laboratory findings revealed increased liver enzymes (AST 220 ALT 70 U/L; peak level AST 6020, ALT 2860 at 32 hours), and D-dimers (56923 mcg/L); INR 2.2; hemoglobin 9.6 g/dL. As serum iron concentration was 4636 micrograms/dL, intravenous deferoxamine 10 mg/kg/h for 12 h and Longastatin 0.025 mg/h for 72 h were started. Fresh frozen plasma and concentrated red blood cells were infused together with electrolytic solution and vitamin K. The upper GI endoscopy performed 10 hours after iron ingestion revealed hemorrhagic enteritis and bleeding from the anastomotic loop. Colonoscopy was negative. Twenty-two hours after poisoning, intravenous infusion of N-acetylcysteine was started at 40 mg/kg/h and prolonged for 66 hours. The patient's condition improved and she was eventually discharged from hospital 12 days after the intoxication with a negative upper GI endoscopy and normal laboratory findings. *Conclusion:* Ferrous iron salts are responsible for direct corrosive effects on GI tract and are absorbed from the small and large intestine. Once absorbed, free iron can catalyze redox reactions with free radical formation and lipid peroxidation leading to possible acute liver failure. Hence, the association of an iron chelator and a free radical scavenger should be considered in order to prevent free radical secondary damage in iron poisoning.

60. Paradichlorobenzene Induced Leukoencephalopathy

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Objective: Although neurotoxicity from chronic paradichlorobenzene (PDCB) exposure is very rare, myelin toxicity and leukoencephalopathy are reported. Only two published case reports of neurotoxicity quantitatively confirm exposure, both with concentrations of PDCB in serum. We report a case of severe leukoencephalopathy confirmed with a PDCB concentration. *Case report:* A 44 year-old man with a history of pica was brought to the ED for 4 weeks of altered mental status and bizarre behavior. He had an atypical aromatic body odor, and was catatonic. He had no psychiatric history or significant drug use. Physical examination was remarkable for lower extremity cogwheel rigidity and hyperreflexia, and scaling skin. Laboratory tests revealed only microcytic anemia (hemoglobin 9.9 g/dL, MCV 72.9 fL) and a urine screen for drugs of abuse was negative. MRI demonstrated hyperintensity of the periventricular white matter. Antibiotics, acyclovir, antipsychotics, mood stabilizers, and antiepileptics produced no response. He deteriorated over two months, at which time his sister revealed that he would eat, huff, and "smoke" mothballs containing 99.99% PDCB. A serum PDCB concentration at that time was 1.2 µg/mL. Approximately six months later, moderate recovery enabled his transfer to a chronic care facility. *Discussion:* Measures of PDCB exposure are difficult to interpret and assistance from detailed case reports is lacking. One previous case reported leukoencephalopathy with a serum PDCB concentration of 34 µg/mL after acute on chronic exposure, while a second reported a serum PDCB concentration of 0.50 µg/mL after two weeks and 0.39 µg/mL after one month of abstinence. Although human toxicokinetic data on PDCB is limited, the half-life in acutely exposed rats is reported as 7.6 hours. Elimination may be slower following chronic administration because an adipose reserve continually releases PDCB leading to prolonged detection in biological samples. Persistent neurotoxicity is typically caused by chronic exposure, and serum concentrations may be low despite apparent toxicity. *Conclusion:* Severe neurotoxicity may occur from chronic PDCB exposure and serum PDCB concentration may remain detectable long after removal from exposure. Until further data is available, PDCB leukoencephalopathy remains a diagnosis of exclusion, relying on history, clinical neurotoxicity and MRI findings.

61. Deliberate Selfharm by Intravenous Injection of Copper and Cyanide

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Objective: To report a case of deliberate selfharm by intravenous injection of copper and cyanide. *Case report:* A 49 year old male laboratory technician presented 6 days after the alleged self-injection into the left antecubital vein of Drabkin's Reagent 25 mL (consisting of Benedict's Solution 25 mL (consisting of crystalline copper sulphate 17.3 gram, sodium citrate 173 grams and sodium carbonate 100 grams dissolved in 700 mL of distilled water, made up to 1000 mL), in his laboratory. He was unconscious for 45 minutes following injection and regained consciousness after treatment in a local clinic. He had been having suicidal ideas for 1 week. Physical examination: Conscious, oriented, pale and icteric, normal vital signs. Cardiovascular and respiratory system - normal. Relevant investigations: haemoglobin 5.4 gm/dL, MCV 107.2, reticulocyte count 10.2, LDH 2464 IU/dL and serum unconjugated bilirubin 5.2 mg/dL, serum copper 354 micrograms/dL (normal range 35 - 232 mcg/dL). ABG - respiratory alkalosis and metabolic acidosis, lactate - 2.2 mmol/L. Peripheral smear - moderate anisopoikilocytosis, polychromatophilia with leucocytosis. In our hospital he received vitamins, folic acid, antibiotics and blood transfusion. Five days after admission he improved, was transferred under psychiatry and discharged 9 days later. He was not treated with chelating agents due to late presentation 6 days after toxin exposure. *Conclusion:* This case is reported because of the unusual presentation with intravenous copper-induced hemolysis and intravenous self-injection of cyanide. *References:* 1. Nelson LS. Copper. In: Goldfrank LR, Flomenbaum N, Levin N, eds. Goldfrank's Toxicologic Emergencies. 7th ed. New York, USA: McGraw-Hill, 2002:1262–71. 2. Narang BS, Reynolds T. Clinical pathologies and urine analysis. In: Medical Laboratory Technology - A procedure manual for routine diagnostic tests. 20th reprint. New Delhi, India: Tata McGraw Hill Publishing Company Limited, 2006:825. 3. Rusia U, Sood SK. Routine haemotological tests. In: Medical Laboratory Technology - A procedure manual for routine diagnostic tests. 19th reprint. New Delhi, India: Tata McGraw Hill Publishing Company Limited, 2006:232.

62. Cyclohexylamine Induced Subdermal Chemical Burns with Persistent Disability

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Objective: Cyclohexylamine is a weak sympathomimetic amine derivative of cyclohexane that is commonly used in rubber, paint, nylon and pesticide industries. It is a weak alkaline chemical known to have irritant properties.[1,2] We present a case of cyclohexylamine induced chemical burns resulting in prolonged functional disability. *Case report:* A previously healthy 22-year-old male employed as a chemical blender in a local industrial plant slipped and fell into a pool of cyclohexylamine, which had leaked onto the floor from a barrel. His personal protective equipment included knee high rubber boots, denim pants and a hip length rain jacket. He immediately removed contaminated clothing and began showering within 60 seconds. Emergency personnel continued decontamination for a total of 30 minutes. During transport he experienced moderate respiratory distress along with nausea and two episodes of emesis. These symptoms quickly resolved with supplemental oxygen and an anti-emetic. His total burn area was estimated at 17%: posterior thighs and buttocks (14%), right scapula (2%) and left frontal scalp (1%). On primary survey the burns were felt to be superficial. However, over the next 6 hours the areas of chemical exposure developed hyperpigmentation which is indicative of sub-dermal penetration. pH testing of the burned areas reflected a value of 10 despite multiple soap and water cleansings. He was discharged after approximately 36 hours of inpatient wound care. On telephone follow-up six weeks later, he was unable to return to work due to severe disabling pain with ambulation. He described hyperpigmentation in the central portions of his wounds. The margins had blanched lighter than the surrounding skin. *Conclusion:* Brief dermal exposure to cyclohexylamine (unknown concentration) resulted in significant cosmetic and functional disability. No other occurrence of subdermal alkali burns with cyclohexylamine was found in a search of the literature. *References:* 1. Carswell TS, Morrill HL. Cyclohexylamine and Dicyclohexylamine. Ind Eng Chem 1937; 29:1247–51. 2. Bopp B. Toxicological aspects of cyclamate and cyclohexylamine. Crit Rev Toxicol 1986; 16:213–306.

63. Unusual Complication of Suicidal Intoxication with a Combined Hypotensive Drug - a Case Report

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Objective: Drug intoxication can result in several medical complications, however, limb amputation is a rare side effect. *Case report:* We present a 46-year old man who had ingested a "handful" of Tarka (capsules containing 2 mg of trandolapril and 180 mg of verapamil) and alcohol with suicidal intent. The patient was found unconscious after 7 hours of sitting in his own car. His left leg was bent at 110 degrees, right leg at 90 degrees, and the trunk was bent forward and lying on the steering wheel. At admission deep coma (GCS 5), hypotension (60/30 mmHg), acute kidney injury and respiratory insufficiency were observed. The skin of both legs was cold and pale, without noticeable tension, and swelling. Laboratory results showed elevated levels of serum creatinine (1.93 mg/dL), creatinine kinase (43868 U/L), D-dimer (6110 ng/mL), and decreased platelet count (60 G/L). USG Doppler examination showed no blood flow bilaterally in the shanks' arteries. Despite aggressive supportive treatment, and hemodynamic improvement, progression of acute ischemia, no power, sensation and reflexes in either leg were observed. The above knee amputations had to be performed in the next few days. *Conclusion:* According to the best of our knowledge there are only few reports of limb amputation because of acute poisonings. Most of them had been associated with narcotics and ergotamine intoxications.[1,2] The fatal posture, vasospasm and compartment syndrome are supposed to be the main causes of amputation in those cases. In our patient, except for the prolonged sitting with bent legs, the most important factor seemed to be profound and long lasting hypotonia which was responsible for acute ischemia of an extremity, tissue necrosis, and further complications. *References:* 1. Musikatavorn K, Suteparuk S. Ergotism unresponsive to multiple therapeutic modalities, including sodium nitroprusside, resulting limb loss. Clin Toxicol 2008; 46:157–8. 2. O'Connor G, McMahon G. Complications of heroin abuse. Eur J Emerg Med 2008; 15:104–6.

64. Successful Treatment of a Dinitrophenol Overdose

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Background: Dinitrophenol (DNP) was first used in the 1930s as a weight loss agent, but fell out of favor as a result of sudden deaths and cataract development with chronic use.[1] DNP is currently used as an insecticide. DNP causes excessive heat production by the uncoupling of the oxidative phosphorylation in mitochondria. Gluconeogenesis, increased anaerobic glycolysis, and lipolysis are the result, resulting in weight loss. Several case reports indicate that DNP intoxication may often be fatal.[1] Severe cases exhibit hyperthermia, seizures, coma, pulmonary oedema, dysrhythmias and renal and hepatic injury. We report a case of severe DNP

poisoning. *Case report:* A 20 year old female presented 4 hours after ingestion of 600 mg of 2,4-dinitrophenol (DNP). She had bought the DNP illegally from the Internet, and was taking 400 mg bd for weight loss. Her regular medication included fluoxetine 60 mg daily. In the Emergency Department she felt unwell and complained of myalgia. On examination there was generalised erythema, profuse diaphoresis, and Kussmaul breathing. Vitals signs were: Respiratory rate 35 bpm, BP 170/70 mmHg, sinus tachycardia 140/min, GCS 15, tympanic temperature 38.5 C. Biochemistry revealed a respiratory alkalosis (pH 7.49, bicarbonate 20.9 mmol/L) marked rhabdomyolysis (CK of 18,000) and a mild rise of AST 463 U/L and ALT 136 U/L. Despite evaporative cooling the temperature continued to rise. The patient was intubated, placed on a cooling mattress and intravenous dantrolene was administered. The CK rose to 30,000 on day two. On day 5 the CK began to fall below 10,000 and the sedation and dantrolene were stopped. She was then extubated. No renal or other organ failure resulted, and the patient was discharged well. Comprehensive toxicology testing revealed therapeutic concentrations of diazepam, fluoxetine and pantoprazole. Cannabis was also detected. *Conclusion:* Our patient was successfully treated with aggressive mattress cooling, intubation, sedation and the early use of dantrolene. *References:* 1. Hsiao AL, Santucci KA, Seo-Mayer P, et al. Pediatric fatality following ingestion of dinitrophenol: postmortem identification of a "dietary supplement". Clin Toxicol (Phila) 2005; 43:281–5.

65. Foodborne Disease After Consumption of Pine Nuts: Data from the French Poison Centres

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Objective: A dysgeusia related to pine nuts consumption was first reported in Belgium in 2000, and identified in France in July 2008 by the French poison centres. This paper aims to describe and analyse the cases reported to the centres, in order to support future decisions. *Methods:* Analysing the notifications related to pine nut consumption reported by the French poison centres based on the CAPTV database. *Results:* Between March 2008 and October 2009, the French poison centres received 2858 calls related to pine nuts consumption. An in-depth analysis of the cases reported between June 15 and September 27, 2009 identified 2225 notifications, among which 70% (N = 1567) were symptomatic cases. These cases were mainly situated in the Paris region (580, 37%) and in the South of France (495, 31.6%). The M/F sex-ratio was 0.66 (587/976). All age groups were concerned, and the most affected was the 30–39 years group who represented 29% of symptomatic cases. 87.5% (N = 1 371) of them had a dysgeusia. The median period before onset of symptoms was 24 hours. The median duration of symptoms was 3 days (ranging from one hour to 14 days). The median quantity of pine nuts ingested was 60 grams, or 2.1 ounces (1 - 800 grams, equiv. 0.035 - 28.22 oz). It seemed likely that the cause of the disease was the ingestion of pine nuts in 1062 cases (89.8%). *Conclusion:* The first results underline a large number of food poisonings due to pine nuts in France in 2009. A certain number of clinical characteristics were documented: long period of time before onset of symptoms (median of 24 hours), spontaneous healing, great interindividual differences. The long-lasting duration of the dysgeusia suggests a possible neurotoxic or lesional process. The pathogenic agent could be a toxin that can be found in some pine nut varieties. Experimental and analytical studies will be needed to confirm or invalidate these hypotheses. *References:* 1. Mostin M. Taste disturbances after pine nut ingestion. Eur J Emerg Med 2001; 8:76.

66. Metabolic Acidosis in Acute Poisoning

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Introduction: Metabolic acidosis in acute poisoning is a common syndrome that is not well studied. In this study we have tried to evaluate the frequency, the mechanisms, the causes, the prognostic factors and the treatment modalities of this abnormality. *Methods:* A prospective observational trial during a nine-month period including all the patients hospitalized for an acute poisoning in our intensive care unit. Two groups have been identified: G1; patients who have a pure metabolic acidosis on admission (pH < 7.37; HCO_3^- < 22 meq/L and $PaCO_2$< 37 mmHg) versus G2; those who have no acid-base abnormalities in the blood gas sample. *Results:* 241 patients were enrolled. Hypobasemia was present in 125 patients (51.9%); 60 of them (24.9%) had a concentration of HCO_3^- < 20 meq/l and 47 (19.5%) had a pure metabolic acidosis. In this last group the anion gap was high in 44 cases (17 lactic acidosis; 22 non lactic acidosis). The characteristics of the two groups and the comparative analysis are summarized in the Table 1. *Conclusion:* This study shows that metabolic acidosis is a frequent abnormality in acute poisoning patients. It can be caused by the nature of the toxic substance itself or related to the severity of the clinical state (shock, hypoxemia). Furthermore we have found that beside the toxic substances usually described, organophosphorus compounds seem to be a non classical cause of metabolic acidosis with unclear mechanism.

Table 1. Characteristics of groups G1 and G2

	G1 N = 47 (19.5%)	G2 N = 56 (23.2%)	p
Age (years)	28.2 ± 14	32.2 ± 16	NS
SAPS II	26.8 ± 13	20.4 ± 13.7	0.048
Admission Delay (h)	10.2 ± 13	5.4 ± 6.6	0.033
Medicaments	19 (40%)	31 (55%)	NS
Alcohols	9 (19.1%)	1 (1.8%)	0.005
Organophosphorus	7 (15%)	1 (1.8%)	0.022
Carbon monoxide	2 (4.3%)	2 (3.6%)	NS
Caustic substances	1 (2.1%)	5 (8.9%)	NS
Coma (GCS<9)	14 (29.8%)	14 (25%)	NS
Shock	8 (17%)	2 (3.6%)	0.041
Seizure	2 (4.3%)	5 (8.9%)	NS
Hypoxemia	12 (25.5%)	3 (5.4%)	0.004
Mechanical ventilation	16 (34%)	21 (36%)	NS
Length of stay (h)	59.5 ± 75	56.2 ± 98	NS
Death	3 (6.4%)	1 (1.8%)	NS

67. The Agent Profile: Sixteen Attributes as a Framework for Risk Determination and Response to Agents of Opportunity in Academic Medical Centers

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Objective: Agents of Opportunity are defined as "dual purpose" substances that are safe when used as intended for medical research and patient care, but potentially harmful if used improperly, whether unintentionally or intentionally. AOs are present in all Academic Medical Centers (AMCs), creating vulnerability. The focus of this research was to identify the most important attributes contributing to AO risk and to produce an Agent Profile for each AO to aid in preparedness for an AO event at an AMC. *Methods:* A literature review was performed to identify existing classification schemes and risk assessment strategies. Attributes identified in 3 seminal classification schemes were considered for inclusion. A final attribute list, affirmed by local experts, aided in the creation of the Agent Profile for each AO, structured after the National Infrastructure Preparedness Plan of the United States. *Results:* Sixteen attributes were identified from the 3 seminal schemes: class, availability, dispersion, exposure/transmission routes, prior events, morbidity/mortality, toxicity, psychological impact, physical state(s), persistence, latency, prevention of exposure, detection, identification, decontamination of building and people, and available treatment. These attributes were sub-classified into: Threat, Vulnerability, and Consequence based on the National Infrastructure Protection Plan with the investigators' addition of Consequence Management. These attributes in this subclassification scheme are compiled into Agent Profiles for each AO. *Discussion:* The Agent Profiles are unique in compiling data across all classes of AOs: biological, chemical, pharmaceutical, and radiological. These profiles can provide assistance in disaster preparedness and response in the pre-event, event, and post-event settings. The Agent Profiles are more encompassing and informative in a wide scale disaster than the traditional Material Safety Data Sheets. *Conclusion:* The Agent Profile permits an AMC to conduct risk assessments across all classes of AOs in a comprehensive manner via the sixteen attributes (subclassified into the threat, vulnerability, consequence, and consequence management).

68. Contact Dermatitis to Dimethyl Fumarate in Seats or Shoes: 118 Cases Notified to the French Toxicovigilance System

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Introduction: Since autumn 2006, numerous cases of severe contact dermatitis to dimethyl fumarate (DMFu) used as a fungicide in seats have been reported in several European countries. In October 2008, the French Ministry for Health asked the Toxicovigilance system to evaluate the risks of human exposure to DMFu. *Methods:* Alert messages were sent to all Dermatology and Emergency units of French hospitals asking for notification of all cases to poison and/or toxicovigilance centres. The notified cases were analysed and classified according to imputability (certainly, probably, possibly, not due to DMFu) based on proof of exposure, symptoms and their chronological association with exposure and the results of patch-tests with DMFu. *Results:* One-hundred and thirty-four cases (134) of possible adverse effects to DMFu-treated materials were notified from the 1st of January 2008 up to the 31st of January 2009 and analysed: 16 were considered

as not due to DMFu, 28 as certainly, 8 as probably, and 61 as possibly due to DMFu; 21 were not classifiable. The items implicated were mostly shoes or boots (55%) and arm-chairs or sofas (39%). In many cases of this series, the data collected did not allow discrimination of allergic from irritative mechanisms of the dermatitis. After eradication of the identified source of exposure, symptoms totally (65%) or partially (26%) resolved in most cases, but persisted in a few patients. *Conclusion:* This series of cases and the review of literature established that DMFu was possibly responsible for both irritative and allergic contact dermatitis. Similar cases were previously also reported with other alkyl fumarates or maleates, with possible allergic cross-reactions. After cessation of exposure, complete healing is the rule. However, in some cases, the persistence of lesions after the apparent eradication of the source suggests allergic reactions from secondary deposits of DMFu. A complementary study is in progress to document this point. DMFu-treated items were recently prohibited in France and the EU. This disposition could prove to be inefficient if fungicide treatment with other alkyl fumarates or maleates is not simultaneously forbidden.

69. Dioxin Contamination of Irish Meat in 2008

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Objective: To describe the discovery of dioxins in Irish pig meat exported to Europe in 2008 and how the source was identified. To analyse the potential hazard to human health of this episode. *Case report:* On Saturday 6th December the Irish Government ordered the recall of all Irish pork products because of fears that the meat had been contaminated. The Food Safety Authority had identified a pig with high polychlorinated biphenyls (PCBs) from a sample taken on November 19th. Investigation of the farm the pig had come from found contaminated feed stuff and subsequently several further farms were identified and closed. The RIKILT-Institute of Food Safety laboratory in the Netherlands identified contaminants in pork products in France, Belgium and Holland as being from the same source. As it was impossible to identify which pork came from the nine contaminated farms all Irish pork products had to be recalled. A Belgian rendering plant stated that they had noticed increased levels of PCBs in September so the recall was backdated to then. The feed mill was identified and heating oil found to be the source of the PCBs. The European Food Safety Authority (EFSA) was available to help with the crisis and analyse the risk to health. They calculated that 6–7% of total pork production in Ireland was contaminated. EFSA established a tolerable weekly intake (TWI) of 14 pg WHO-TEQ/kg body weight for substituted PCDDs and dioxin like PCBs. They calculated that the body burden would increase by 10% for an Irish consumer who had eaten pork at the highest contaminated level measured (200 pg TEQ/g fat) during the 90 days of possible exposure and this represented a low risk to health.[1] A similar incident in Belgium in 1999 was calculated to have caused an increased body burden for PCBs of 42%.[2] *Conclusion:* Prompt recall of contaminated pork prevented exposure of the population to dangerous levels of dioxin. Cooperation from EFSA and European laboratories was important in managing the crisis. *References:* 1. Statement of EFSA on the risks for public health due to the presence of dioxins in pork from Ireland. EFSA Journal 2008; 911:1–15. 2. Van Larebeke N, Hens L, Schepens P, et al. Belgian PCB incident. Environ Health Perspect 2001; 109:265–73.

70. Serotonin Syndrome Induced Solely by Carisoprodol Overdose

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Objective: A variety of medications have been known to induce serotonin syndrome (SS), with MAOIs or SSRIs most commonly implicated. We report a case of SS after ingestion of carisoprodol alone. *Case report:* A 40 year old woman was brought to the ED for altered mental status several hours after the witnessed ingestion of a "handful" of carisoprodol. Fifty-eight tablets of 350 mg carisoprodol were ingested over the preceding 6 days. Other medications included only oxycodone/acetaminophen, with no evidence suggesting ingestion. On presentation, the patient was confused and nonverbal, exhibiting difficulty moving her extremities. Physical exam revealed tachycardia, mild hypotension, mid-to-small reactive pupils, and dry skin. Neurological exam revealed tremor, hyperreflexia, increased tone, and bilateral inducible ankle clonus. EKG ST 113 with normal axis/intervals. Salicylate, acetaminophen, and ethanol levels were undetectable, and urine drug immunoassay tested positive only for benzodiazepines, administered after arrival. Head CT was unremarkable. A diagnosis of SS was made based upon the Hunter criteria, and the patient was started on cyproheptadine in conjunction with benzodiazepine therapy.[1] Serum CKs were monitored for rhabdomyolysis, reaching a peak of 519 U/L. The patient made a full recovery over the next 24 hours. *Conclusion:* A variety of medications, often when used in combination, have been implicated as causative agents of SS, presumably based on their degree of 5-HT2A agonism. While a list of such serotinergic drugs can be extensive, it is rare for this condition to be caused solely by non-MAOI/SSRI medications. Carisoprodol and its metabolite meprobamate are believed to exert their actions at the GABA-A receptor, and are not widely known to result in SS.[2] This case suggests carisoprodol may have additional pharmacologic properties that alone in overdose may result in a syndrome meeting diagnostic criteria for SS. Clinicians should be aware of this possibility from such an atypical source. *References:* 1. Dunkley EJC, Isbister GK, Sibbritt S, et al. The Hunter Serotonin Toxicity Criteria: simple and accurate diagnostic decision rules for serotonin toxicity. QJM 2003; 96:635–42. 2. Boyer EW, Shannon M. The serotonin syndrome. N Engl J Med 2005; 352:1112–20.

71. Immunohistochemical Study Effects of Methamphetamine on Proliferation and Apoptosis of Sperm Germ Cells in Mature Rats

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Introduction: Methamphetamine (MAMP) is a central nervous system stimulant that is increasingly abused by teenagers and young adults. MAMP effects on the male reproductive system are not clear. In this experimental study, we evaluated the effects of a single injection of three different doses of MAMP on proliferation and apoptosis in the sperm germ cells of mature rats. *Methods:* Four groups of mature rats were injected IP with three doses of a single dose of MAMP (1, 5 or 15 mg/kg) or normal saline. The right and left tissue sections were immunostained with immunohistochemical methods for proliferation and apoptosis, respectively. Indexes were calculated for proliferating and apoptotic cells. *Results:* Cell proliferation decreased significantly in the group with the highest dose. The ratio of proliferation to apoptosis decreased significantly in two groups with the highest doses. Conversely, apoptosis occurrence was increased in these groups. In the control group, more than 95% of spermatogonia were proliferating cells, however, 15 mg/kg of MAMP caused a 85% reduction in the number of proliferating spermatogonia. On the contrary, the number of apoptotic cells at least doubled in some tubules of these groups. There were significant differences between the lower dose group and the higher doses groups. Therefore, the observed differences were relatively dose-dependent. *Conclusion:* This study revealed that one exposure to MAMP, particularly at the high dose, can change the proliferation/apoptosis ratio in rat testis. Therefore, this would adversely affect the normal spermatogenesis process and this could lead to disturbances in male fertility.

72. Neuropsychiatric and Other Adverse Reactions to Oseltamivir (Tamiflu)

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Objective: In 2009, oseltamivir (Tamiflu, Roche Products Australia) began to be used at unprecedented levels in Australia and worldwide. Neuropsychiatric reactions to oseltamivir have been reported in the past, predominantly from Japan. This case series describes two cases of neuropsychiatric reactions and summarises adverse reactions reported from oseltamivir in Australia. *Case series:* Patient 1 - A previously healthy 4 year-old boy with suspected H1N1 influenza 09 was prescribed oseltamivir 48 mg twice daily, the first and only dose was administered at 7 pm. After a few hours of sleep the child awoke unsettled and agitated with visual hallucinations. He was calmed by his mother and eventually fell asleep to wake again at midnight with continued abnormal behaviour, incoherent speech and visual hallucinations. His temperature in the first instance was 38.1°C and the second 36°C. The child continued to visualise stationary objects as moving into the morning. The only medications used recently for this child were ibuprofen and paracetamol in regular doses. Patient 2 - A previously healthy 43 year-old man with suspected H1N1 influenza 09 was prescribed oseltamivir 75 mg twice daily, with the first and only dose taken at 7.30 pm. Within 1.5 hours he was noted by his partner to be behaving unusually with incoherent speech, aggression, confusion and limb twitching. The reaction resolved within 2 hours and the following morning the patient had no recollection of the evening's events. In the period January to October 2009, two milder neuropsychiatric reactions, five cases of nausea, 20 of nausea with vomiting and four cases of hypersensitivity reactions have been reported to the NSW Poisons Information Centre. In January to August 2009, the Therapeutic Goods Administration received five voluntarily submitted reports of possible neuropsychiatric reactions, five cases of vomiting and 13 suspected hypersensitivity reactions. *Conclusion:* Oseltamivir use may be associated with serious but uncommon adverse events such as neuropsychiatric and hypersensitivity reactions. In particular, adverse drug reaction should be considered in the differential diagnosis of transient delirium developing in patients taking oseltamivir. Health professionals prescribing or dispensing oseltamivir need to be aware of its side effects and ensure that adequate information is provided to patients.

73. Admissions to the Medical Emergency Department due to Intentional Medication Overdoses, Medication Errors and Adverse Drug Reactions

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Objective: Intentional medication overdoses, medication errors (MEs) and adverse drug reactions (ADRs) have been regarded as a major public health problem as they represent a sizable percentage of admissions to emergency departments (EDs). The aim of this study was to evaluate the frequency of admission to EDs and hospitalization due to medication detected by emergency physicians. *Methods:* The study team of internal medicine specialists retrospectively reviewed 1000 randomly selected medical records out of 23,000 patients treated at the primary city and tertiary referral governmental hospital ED in 2009 for ADRs, MEs and intentional medication overdoses detected by emergency physicians during patient presentation. *Results:* The established frequency of admissions at the ED due to intentional medication overdose was 1.3% of all patients (13/1000). Intentional overdose of benzodiazepines was the most common cause of ED admissions (6/13). One per cent (1.0%) of all patients admitted at the ED (10/1000) required hospitalization due to intentional medication overdose. The frequency of ED admissions due to MEs was 1.2% of all patients (12/1000). Unintentional overdose

of digoxin, warfarin, insulin and theophylline and deliberate discontinuation of antihypertensive medications, proton pump inhibitors and insulin were the most common causes of ED admissions due to MEs. 0.4% of all patients admitted at the ED (4/1000) were hospitalized due to MEs caused by warfarin, digoxin and insulin. The frequency of ED admissions due to ADRs was 3.7% of all patients (37/1000). Bradycardia due to verapamil, digoxin and beta-blockers was the most common ADR and represented 20% of all ADRs. 0.5% of all patients admitted at the ED (5/1000) were hospitalized due to ADRs caused by beta-blockers, digoxin, diuretics, NSAID, acetylsalicylic acid, clopidogrel, and tamoxifen. *Conclusion:* Medications cause 6.2% of all admissions to the medical ED. 1.9% of all patients admitted to the medical ED are hospitalized due to medication, which represents 5.9% of hospitalized patients through the medical ED to internal medicine departments (19/320). Intentional overdose caused 20% of all ED admissions and 50% of all hospitalizations due to medication. *Acknowledgment:* This study was in part supported by a grant from Zavod za zdravstveno zavarovanje Slovenije (UL RS, st 9/2009, 06/02/2009).

74. Impact of Risk Minimisation Measures for Buflomedil: A 2-year Surveillance from the French Poison and Toxicovigilance Centres

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Objective: Buflomedil (150 and 300 mg per tablet) is a vasoactive agent used in France for peripheral arterial obstructive disease since 1976. A retrospective study (RS) of poisoning cases reported to the French poison centres (1998–2004) had shown severe neurologic and cardiovascular effects and led to taking risk minimisation measures: withdrawal of the 300 mg tablets (November 2006), restriction of indications and implementation of a "post risk minimisation" prospective study (PS). The objective was to evaluate the impact of these measures by comparing the RS and the PS (2007–2008). *Methods:* All poisoning cases involving buflomedil reported to the French poison and toxicovigilance centres (2007–2008) were analysed. The number of suicidal attempts, severe cases (convulsions, status epilepticus, severe cardiac troubles) and deaths were compared (Chi2/Fisher's exact, Mann-Whitney tests). Results were adjusted on sales (boxes) and prescription data and compared using Poisson test. *Results:* In the PS 25.5 annual suicidal attempts cases were registered versus 32 in the RS ($p = 0.46$). Severe cases were respectively 39% and 45% ($p = 0.47$), and deaths respectively 5.9% and 10.0% ($p = 0.28$). Surprisingly, there were 8 poisoning cases with 300 mg tablets in the PS (1 case in 2007 and 7 in 2008). To take into account the "future" benefit of the dosage reduction, cases involving 150 mg tablets were analysed separately. The adjustments on sales (0.22 cases per 100,000 sold boxes in the PS, versus 0.20 per 100,000 in the RS; $p = 0.27$) and prescriptions (1.9 per 100,000 prescriptions versus 2.1 per 100,000; $p = 0.58$) did not show significant differences between the 2 studies. Regarding the proportion of severe cases, there were also no differences between the PS (30%) and the RS (33%), when only cases with 150 mg tablets were considered ($p = 0.75$). *Discussion:* Data from poison centres can be used to estimate the impact of the risk minimisation measures. In these successive studies, the level (and the stability) of the proportion of severe poisoning cases with buflomedil 150 mg tablets indicate that the residual risk after withdrawal of 300 mg tablets is still high. These data call for a re-evaluation of the buflomedil risk profile.

75. Neuroleptic Malignant Syndrome Variant in a Child on Aripiprazole

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Background: Neuroleptic Malignant Syndrome (NMS) is a condition of altered mental status, fever, muscle rigidity, and dysautonomia that can occur due to decreased dopaminergic activity. We report a case of a child who developed NMS-like manifestations after initiating aripiprazole, an atypical antipsychotic with agonist/antagonist activity at central dopaminergic and serotinergic receptors. *Case report:* An 8 year old with Attention Deficit Hyperactivity Disorder (ADHD) and bipolar disorder was started on aripiprazole (10 mg qhs). Other routine medications included: clonidine, valproate (discontinued when aripiprazole was started), cyproheptadine, and methylphenidate. After two doses of aripiprazole he developed confusion, ataxia and drooling. He was seen at a hospital and instructed to stop aripiprazole and start benztropine 0.5 mg daily. Three days after stopping aripiprazole, and despite benztropine (0.5 mg), the child worsened with unresponsiveness, severe lead pipe rigidity, and urinary incontinence. On examination the child had hyperpyrexia (101 °F), tachycardia (130–150 bpm), and hypertension (SBP 140–170 mmHg). Pupils were 6 mm and minimally reactive. Saliva pooled in his mouth. Bowel sounds were decreased. Reflexes were normal; there was no clonus. All four extremities had lead pipe rigidity. With any verbal or tactile stimulation, he developed painful, intermittent, tonic truncal and extremity muscle spasms. CPK was mildly elevated (peak 852 IU/L). Other studies were normal including electrolytes, renal function, glucose, urine drug screen, urinanalysis, CT brain, and lumbar puncture. During hospitalization, Tmax was 101 °F. Treatment included lorazepam (5.5 mg IV total) and restarting clonidine. Altered mental status, muscle rigidity, and spasms completely resolved over three days. *Conclusion:* NMS-like manifestations developed after two doses of aripiprazole. The child had unusual rigidity, mild CPK elevation, and mild hyperthermia. Overall, his clinical course was shorter than expected with NMS. As more children are started on atypical antipsychotic medications, more NMS variants may be seen.

76. Severe Toxicity of a Single Therapeutic Dose of Baclofen in Patients with Impaired Renal Function

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Objective: To describe the occurrence of toxic effects of baclofen after ingestion of single therapeutic doses in adult patients with renal failure. *Methods:* Analysis of all cases of oral baclofen adverse drug reactions in adults with confirmed renal impairment reported to a Poisons Information Centre between 1966 and 2008 with written medical feedback and sufficient causality. *Results:* Three cases fulfilled all inclusion criteria. All patients experienced severe symptoms (Table 1). *Discussion:* According to the literature the minimum single oral dose of baclofen for severe toxicity in adult patients with normal renal function is 200 mg.[1] Severe toxicity of baclofen has been frequently reported in the literature in patients with impaired kidney function after repeated ingestion of therapeutic doses. Accumulation of baclofen due to diminished renal elimination has been postulated as the main pathophysiologic mechanism.[2] Our patients presented with severe toxicity immediately after ingesting the first therapeutic dose (25–50 mg) of baclofen. Concomitant medication was unchanged. *Conclusion:* In our case series the patients experienced severe toxicity after a first low oral dose of baclofen. This suggests that not only accumulation, but also other underlying mechanisms may play a role, such as altered pharmacodynamics associated with renal failure or interacting co-medication. Further studies are needed to investigate possible pathophysiological mechanisms of severe toxicity of baclofen in renal failure. *References:* 1. Leung NY, Whyte IM, Isbister GK. Baclofen overdose: defining the spectrum of toxicity. Emerg Med Australas 2006; 18:77–82. 2. Chen KS, Bullard MJ, Chien YY, et al. Baclofen toxicity in patients with severely impaired renal function. Ann Pharmacother 1997; 31:1315–20.

Table 1. Three patients with severe symptoms after low dose baclofen

Patient	Dose ingested	Renal function	Symptoms
45 yo male	50 mg	Chronic renal failure	Coma, muscular spasms
42 yo male	25 mg	Diabetic nephropathy (diabetes mellitus type 1)	Coma, hyperreflexia
58 yo male	40 mg	Chronic renal failure	Coma

77. Acute Laryngotracheitis after Accidental Aspiration of Clindamycin

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Objective: Capsular clindamycin is frequently used to prevent infections after dental surgery. The occurrence of esophagitis and esophageal ulcers has been previously described.[1] Recently our poison centre was notified about a case of accidental aspiration of the capsule content with subsequent laryngotracheitis. Our database contains four further cases of adverse events due to aspiration of the content of clindamycin capsules. To our knowledge no comparable cases have been published to date. *Case report:* A 78-year-old patient was treated with capsular clindamycin (150 mg cps) after dental implantation. One capsule, swallowed with a small amount of water, accidentally opened during ingestion with subsequent aspiration of the content. The patient immediately reported burning throat pain. He progressively developed respiratory distress and had a syncopal episode at admission. Initial laryngoscopy showed acute laryngotracheitis, moderate inflammatory edematous change of mucous membrane between oropharynx and trachea, two subglottal, hemorrhagic lesions and bilateral chalky, whitish plaques in the sinus piriformis and vallecula. Temperature was 38 °C (100.4 °F), leucocytes 14.2 G/L, C-reactive protein 73 mg/mL. The chest X-ray showed discrete signs of aspiration. Methylprednisolone, clemastine, and amoxicillin / clavulanic acid were administered. Control laryngoscopy after three days of treatment showed persistent slight subglottal swelling and spot-shaped whitish coating and slight supraglottal fibrin coatings. The clinical course was favourable; the patient was discharged asymptomatic at the fifth day. Steroids were discontinued after five days, antibiotics after ten days. A follow-up examination on the 9th day showed *restitutio ad integrum*. *Case series:* Four similar cases were identified in our database (1995–10/2009). The symptoms reported were burning pain (2 cases), cough (3), nausea (3), dyspnea (2), aphonia (2) and syncope (1). *Conclusion:* The accidental opening of clindamycin capsules during swallowing can lead to severe laryngotracheitis. Patients should be advised of this hazard. The risk of aspiration may be minimized if the drug

is ingested with a sufficient amount of liquid. *References:* 1. Jaspersen D. Drug-induced oesophageal disorders: pathogenesis, incidence, prevention and management. Drug Saf 2000; 22:237–49.

78. Co-Proxamol Withdrawal - Five Years On

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Objective: Co-proxamol (paracetamol 325 mg and dextropropoxyphene 32.5 mg) was previously one of the most commonly prescribed analgesic agents in the UK. However, following evidence of increased mortality in overdose and a lack of analgesic benefit over other simple analgesics, co-proxamol underwent a phased withdrawal from the UK market in 2005. Similar recommendations have now been implemented across Europe. We previously demonstrated the initial effect of this legislation on Scottish mortality figures and similar results have been shown elsewhere in the UK. We have now extended the study period to assess the longer-term effect of legislation on mortality in Scotland from poisoning with co-proxamol and other similar agents. *Methods:* Mortality data relating to poisoning by single agents in Scotland were obtained from the General Register Office for 2000–08. Deaths due to co-proxamol poisoning alone (± alcohol) were identified and those involving multiple agents were excluded. Proportional co-proxamol mortality before and after legislation was compared. Primary care prescribing data was obtained from the Information and Statistics Division of the Scottish Executive Health Department. *Results:* Following legislation mortality associated with co-proxamol poisoning in Scotland has significantly reduced beyond that already reported (mean 2000 - 04, 37 deaths (21.8% of total poisoning deaths); 2008, 2 deaths (1%); $p < 0.0001$). The decline in mortality has been associated with a precipitous fall in co-proxamol prescriptions, with a steady rise in prescriptions for co-codamol and paracetamol. No concomitant rise in mortality from poisoning with these, or any other analgesic agents, was identified. *Conclusion:* We have demonstrated a reduction in mortality from co-proxamol poisoning following legislation. Despite a steady rise in prescriptions for paracetamol and co-codamol, there is no evidence of increased mortality associated with these agents. We estimate that across the UK more than 300 lives per annum will be saved following legislation to withdraw co-proxamol.

79. Cholestasis Induced By M-Drol Successfully Treated with Molecular Adsorbent Recirculating System

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Objective: It is known that anabolic-androgenic steroids (AAS) can lead to serious and irreversible organ damage, however, anabolic supplements (AS), which are sold legally, are treated by bodybuilders as safe products with no or minor side effects.[1] According to the best of our knowledge there are no medical reports about toxic cholestasis connected with the usage of AS. *Case report:* A 23-year-old male bodybuilder, with no prior medical history, was admitted to the hospital because of jaundice. According to anamnesis before hospitalization he self-administered two tablets of M-drol (Competitive Edge Labs, ingredients: 2a, 17a dimethyl etiocholan 3-one, 17 b-ol; microcrystalline cellulose, dicalcium phosphate, magnesium stearate, and stearic acid, 10 mg) daily for four weeks. At admission the serum bilirubin level was 13.9 mg/dL, aspartate transferase 115 IU/L, alanine transferase 413 IU/L, prothrombin time 102%, gamma-glutamyl transferase 64 IU/L, and alkaline phosphates 114 IU/L. Despite aggressive supportive treatment, the bilirubin level increased up to 30.0 mg/dL, and invalidating pruritus was observed. Five sessions of MARS, which lasted six hours each, were conducted every second day.[2] The procedure was well tolerated by the patient and resulted in a sustained relief of pruritus as well as in decline of plasma bilirubin to 4.0 mg/dL. The patient was discharged home in good general condition. Two weeks follow up showed that the patient felt very well, and the bilirubin level reduced to 2 mg/dL. *Conclusion:* Anabolic supplements can cause serious side effects. In some cases, where supportive treatment is ineffective, Molecular Adsorbent Recirculating System - MARS gives very good relief for the pruritus. *References:* 1. Maravelias C, Dona A, Stefanidou M, et al. Adverse effects of anabolic steroids in athletes. A constant threat. Toxicol Lett 2005; 15:167–75. 2. Bellmann R, Feistritzer C, Zoller H, et al. Treatment of intractable pruritus in drug induced cholestasis with albumin dialysis: a report of two cases. ASAIO J 2004; 50:387–91.

80. Prolonged Hypertension after Empiric Treatment with Hydroxocobalamin for Presumed Cyanide Toxicity

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Objective: Studies have raised concerns over the effect hydroxocobalamin has on blood pressure caused by nitric oxide scavenging.[1] We present a case of severe and prolonged hypertension following the use of hydroxocobalamin. *Case report:* A 50 year-old man in cardiac arrest following a building fire, received epinephrine 3 mg, vasopressin 40 units, atropine 2 mg, during successful prehospital resuscitation. In the ED, his vital signs were: BP 100/60 mmHg; HR 118 beats/min; RR 12/min; Temp 36.7°C; O_2 saturation 98% on 100% O_2. Post-arrest hypothermia protocol was initiated and a 2L NS bolus improved his BP to 166/68 mmHg. Significant laboratory data include: carboxyhemoglobin, 46%; blood lactate, 11.5 mmol/L. Physical exam: no significant trauma or cutaneous burns, but carbonaceous material was present around his mouth and nares. He received hydroxocobalamin 5 g intravenously as empiric therapy for cyanide. Soon after his blood pressure began to rise peaking thirty minutes later at 220/180 mmHg. Despite sedation with fentanyl and propofol, ninety minutes after hydroxocobalamin his blood pressure remained elevated at 185/79 mmHg. A goal MAP of <110 mmHg was achieved within 45 minutes of initiation of a nicardipine infusion, which was required for 16 hours. The patient was declared brain dead and expired on day 10 after care was withdrawn. A serum sample obtained prior to administration of hydroxocobalamin revealed no detectable concentration of cyanide. *Conclusion:* Hydroxocobalamin is considered a safer alternative to the traditional cyanide antidote kit due to the lack of methemoglobin generation. Hydroxocobalamin causes hypertension in healthy volunteers who are not cyanide poisoned.[1] Although the clinical significance of hypertension in this patient is unclear, his risk of this adverse event was possibly increased because he was not cyanide poisoned. Cautious administration and continued observation of hydroxocobalamin's clinical use in potential cyanide poisoning victims may help identify risk factors for hypertension and other adverse outcomes. *References:* 1. Uhl W, Nolting, A, Golor, G, et al. Safety of hydroxocobalamin in healthy volunteers in a randomized, placebo-controlled study. Clin Toxicol 2006; 44:17–28.

81. Myocardial Arrest Associated with Propranolol Use in Thyroid Storm

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Objective: Thyroid storm is a rare clinical emergency that is fatal when left untreated. Beta-blockers and antithyroid medications are the first-line treatment. We report a fatal case due to propranolol use in thyroid storm. *Case report:* A 39-year-old man presented to the emergency department with a thyroid storm. ECG revealed a paroxysmal atrial fibrillation with a ventricular rate of 214 bpm. Cardiac ultrasound showed a left ventricular ejection fraction (EF) of 35%. The patient was started on propranolol 2 mg i.v. Three hours later, the ECG showed supraventricular tachycardia (110 bpm) and an additional propranolol infusion (5 mg infused at a rate of 0.16 mg/min over 30 minutes) was administered. Because of worsening dyspnea, transthoracic echocardiogram was repeated and revealed a severe reduction of EF to 15%. Three hours after propranolol infusion, the patient developed cardiorespiratory arrest: cardiopulmonary resuscitation was immediately started, but the patient's clinical course was complicated by cardiogenic shock poorly responsive to pharmacological treatment. The patient was transferred to the Coronary Unit for extracorporeal cardiovascular support with ECMO. He remained comatose and anuric; subsequently, he developed multiorgan failure and died 5 days later. *Conclusion:* In hyperthyroid patients, an excess in circulating thyroid hormones may result in an abnormal left ventricular function[1] and under stress some of them can develop low-output heart failure.[2] In thyrotoxic patients, left ventricular ejection fraction decreases after propranolol administration[3] and cardiovascular collapse may be a serious complication following beta-blockade in thyroid storm.[1] In patients with thyroid storm, early EF assessment may guide beta-blocker choice: when low cardiac output is observed, it might be prudent to consider alternative beta-blockers with shorter half-life like esmolol. *References:* 1. Dalan R, Leow M. Cardiovascular collapse associated with beta blockade in thyroid storm. Exp Clin Endocrinol Diabetes 2007; 115:392–6. 2. Forfar JC, Muir AL, Sawers SA, et al. Abnormal left ventricular function in hyperthyroidism: evidence for a possible reversible cardiomyopathy. N Engl J Med 1982; 307:1165–70. 3. Critchley M, Gulliford P. An equilibrium radionuclide technique to assess the effect of propranolol on left ventricular function in thyrotoxicosis. Clin Radiol 1980; 31:717–22.

82. Profiling the Risk to Academic Medical Centers by Agents of Opportunity

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Objective: Agents of Opportunity (AOs) are operationally defined as biological, chemical, radiological, and pharmaceutical substances that can be readily found and disseminated in conventional settings. AOs used for the provision of medical treatment, education, and research present unique risks to healthcare infrastructure due to their potential misappropriation (or misuse) and the intentionally open environment of most Academic Medical Centers (AMCs). Depending on AO and dissemination mode, the impact may be health-, psychological-, or mission-related, affecting the patients, staff, students, researchers, volunteers, visitors, contractors, or community served by AMCs. *Methods:* Using a risk assessment framework promulgated by US Department of Homeland Security,[1] we designed a database linear assessment tool to evaluate AMC vulnerability to twenty previously identified AOs. *Results:* Automated assessment forms permitted customized inputs of AO presence and accessibility based on building-specific acquisition sites (surgical, radiation oncology, nuclear medicine, and chemotherapy units), demographically distinct wards (obstetrics, pediatrics, adults, and geriatric), support areas (microbiological, hematology, and chemistry laboratories; transfusion services; and loading docks), and research space. Selection of these locations launched site-specific agent availability queries (e.g. for inhalational anesthetics and opioids in surgical areas; radionuclides in

nuclear medicine; gastrointestinal, respiratory, or blood borne pathogens in microbiology and transfusion medicine spaces; and acids, bases, and other potentially hazardous chemicals in research spaces). Independent dissemination modalities and access sites included HVAC, pneumatic tube, elevator, and water systems; food services; central and cleaning supplies; and pedestrian surface tracking. Security level assessments integrated security practice (behavior) and access control (engineering) concepts for both agent acquisition and dissemination sites. By pairing AO acquisition and dissemination modes, the Demonstration Version produced vulnerability reports by building, acquisition site, and security level for a variety of AOs. *Conclusion:* An AO profiling instrument can augment the limited health sector specific tools available to assist AMCs with assessment of unique human engineered threats. Future work will address integrating the results with an informational database for education and mitigation efforts. *References:* 1. National infrastructure protection plan: partnering to enhance protection and resiliency. Washington, DC: US Department of Homeland Security, 2009. Published online at http://www.dhs.gov/xlibrary/assets/NIPP_Plan.pdf.

83. Methylphenidate Toxicity: A Study of Dose Dependent Adverse Drug Effects Using Patients with Methylphenidate Overdose

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Objective: A possible link between therapeutic stimulant use and sudden death has been suggested.[1] One potential mechanism is drug-induced repolarisation delay, consequent QT prolongation and ventricular arrhythmias. This has been reported inconsistently with methylphenidate in therapeutic doses.[2] Since repolarisation delay is usually dose related,[3] drug overdose may be a sensitive model for detecting effects, so the effects of methylphenidate in overdose on the electrocardiogram were studied in comparison to a suitable control group. *Methods:* Methylphenidate overdose cases admitted to Newcastle or Edinburgh Poisons Services (2000–2007) were matched for sex and heart rate with a control subject admitted over the same time period with a non-cardiotoxic overdose, mainly paracetamol. Notes were reviewed retrospectively for clinical details. Admission 12-lead ECGs were analysed using a manual digitiser in blinded manner. Mean QRS and QT intervals were calculated and differences between cases and controls analysed. *Results:* There were 23 cases of methylphenidate overdose (10 male, 13 female, mean age 27.8 years, median dose 120 mg [range 40–1500 mg]). Co-ingestants were taken by 17. Cases' level of consciousness and mean haemodynamic parameters were within normal limits and no arrhythmias recorded. Symptoms included anxiety (32%), dilated pupils (20%), abdominal pain (16%), vomiting (12%), palpitations (12%), and chest pain (8%). There were no significant differences between the groups in mean heart rate (92.4 vs. 93.7 /min, difference -1.4, 95%CI -3.1 to 0.3/min), QRS duration (86.1 vs. 86.2, difference 0.1, 95%CI -5.1 to 5.0 ms), or QT interval (354 vs. 355, difference -0.8, 95%CI −10.7 to 9.2 ms). *Conclusion:* Clinically important QT prolongation with therapeutic dose methylphenidate seems unlikely in the absence of effect in overdose. Drug overdose may be a useful model for investigating possible dose-related electrocardiographic drug effects. *References:* 1. Gould MS, Walsh TB, Munfakh JL, et al. Sudden death and use of stimulant medications in youths. Am J Psychiatry 2009; 166:992–1001. 2. Pekdemir H, Toros F, Çamsar A, et al. The effect of methylphenidate on cardiovascular functions in treatment of attention deficit hyperactivity disorder. Çocuk ve Gençlik Ruh Sagligi Dergisi 2003; 10:9–16. 3. Krantz MJ, Kutinsky IB, Robertson AD, et al. Dose-related effects of methadone on QT prolongation in a series of patients with torsades de pointes. Pharmacotherapy 2003; 23:802–5.

84. If Vitamins Could Kill: Massive Hemolysis Following Naturopathic Vitamin Infusion

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Objective: To report a case of a 47 year-old man with massive intravascular hemolysis following a naturopathic vitamin infusion. *Case report:* A 47 year-old African-American man presented to the hospital with three days of fever, dyspnea, emesis, dark urine and progressive confusion. His symptoms began one day following an infusion of a vitamin complex that was given to him by a naturopathic physician. Initial vital signs were: BP 133/76 mm Hg; HR 120/min; RR 16/min; T 37.2°C; SpO_2 100% on RA. His physical examination was significant for lethargy and scleral icterus. Initial laboratory studies were notable for anemia (hemoglobin 33 g/L, hematocrit 11%), brisk reticulocytosis (33%), acute renal insufficiency [creatinine 247.52 µmol/L), and indirect hyperbilirubinemia (total bilirubin 75.24 µmol/L). His peripheral smear demonstrated "blister cells," (erythrocytes that have been left devoid of precipitated hemoglobin by the spleen, commonly seen in glucose 6-phosphate dehydrogenase deficiency). He was admitted with the diagnosis of hemolytic anemia, received a transfusion with 2 units of red blood cells and several plasmapheresis sessions. His outpatient physician revealed that he administered an infusion containing vitamin B and D complex, free amino acids, magnesium and taurine. The patient clinically improved and was discharged to home. Follow-up hemoglobin two weeks later was 84 g/L. His G6PD status will be confirmed following complete recovery. *Conclusion:* We report a case of massive intravascular hemolysis following a naturopathic vitamin infusion in a patient with previously unknown G6PD status. Hemolysis from naturopathic remedies has been reported with high doses of ascorbic acid in G6PD deficient individuals. It is challenging to link this patient's hemolytic crisis to the reported contents of the "vitamin infusion," since neither the full contents nor the method of preparation of this remedy was ever disclosed. Since most properly-formulated naturopathic treatments have little active ingredients, the possibilities of improper formulation, or toxic diluents and contaminants should be considered. Inadequate regulation of naturopathic remedies has the potential to induce serious toxicity, especially in genetically predisposed individuals.

85. Recreational Inhalation of Ethyl Chloride Leads to Neurotoxicity

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Objective: Ethyl chloride is a colorless, volatile gas sold online and in the specialty stores, with uses ranging from a VCR head cleaning solvent to a topical anesthetic to a recreational drug for inhalation. We report a case of neurotoxicity from ethyl chloride inhalation. *Case report:* A 45 year-old man with a history of HIV presented to the hospital with persistent ataxia, difficulty writing, and slurred speech for one day after inhaling approximately eighteen canisters of VCR head cleaning solvent containing ethyl chloride. He has previously reported similar symptoms, though transient, and had a normal brain MRI one month earlier. The patient's initial neurological examination was significant for decreased strength in bilateral hip, knee, foot flexor and extensor muscle groups, and hyperreflexia in both lower extremities. The heel-to-shin maneuver was abnormal and a Romberg test was positive. He had pronounced ataxia and a spastic gait requiring a walker. His speech was slightly slurred but easy to comprehend. Serum B12 and potassium were normal and the brain MRI was not repeated given recent unremarkable imaging. The symptoms gradually improved and he was discharged after five days of hospitalization to follow up with his neurologist. *Conclusion:* Ethyl chloride is a recreational inhalant drug that is usually huffed, or sprayed into a cloth and inhaled. Signs and symptoms noted in the few reported cases of ethyl chloride toxicity include ataxia, lower extremity motor and sensory neuropathy, dysarthria, cerebellar signs, and death from presumed arrhythmogenesis. The clinical findings are similar to those produced by other halogenated hydrocarbons. Given the length of duration of our patient's symptoms, ethyl chloride's excessive or long-term recreational use may lead to prolonged neurotoxicity. *References:* 1. Finch CK, Lobo BL. Acute Inhalant-Induced Neurotoxicity with Delayed Recovery. Ann Pharmacother 2005; 39:169–72. 2. Nordin C, Rosenqvist M, Hollstedt C. Sniffing of ethyl chloride - an uncommon form of abuse with serious mental and neurological symptoms. Subst Use Misuse 1988; 23:623–7.

86. Anabolic Steroid Use Leads to Acute Lung Injury

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Objective: Anabolic steroids are commonly abused by both amateur and professional athletes. We report two cases of acute lung injury associated with intramuscular injection of anabolic steroids. *Case series:* Case 1: A 32 year-old man presented to the hospital with severe respiratory distress one hour following gluteal self-injection of a mixture of testosterone, methenolone and nandrolone. His initial vital signs were: BP 111/75 mm Hg; HR 100/min; RR 31/min; T 98.7°C; SpO_2 74% on 15L O_2. The patient received albuterol, diphenhydramine, dexamethasone, and BiPAP with improved oxygenation. CT chest demonstrated acute lung injury without evidence of a pulmonary embolus. A broncho-alveolar lavage was normal, and the patient recovered fully within a week. Case 2: A 26 year-old man presented to the hospital with dyspnea for four hours. His symptoms started 30 minutes after gluteal self-injection of an anabolic steroid. Vitals signs were: BP 125/79 mmHg; HR 130/min; T 98.7°C; RR 28/min; SpO_2 90% on room air. He was in moderate respiratory distress, with diffuse rales and wheezing. An arterial blood gas revealed: pH 7.41; pCO_2 38 mmHg; pO_2 105 mmHg; saturation 98%; on FiO_2 of 40%. Chest radiograph demonstrated diffuse infiltrates bilaterally. The patient was treated with albuterol, methylprednisolone, and BiPAP. Within 48 hours of hospitalization, the patient recovered fully and was discharged home. *Conclusion:* Two patients developed acute lung injury following intramuscular injection of anabolic steroids. Acute pulmonary symptoms from pulmonary emboli, pulmonary peliosis, and eosinophilic pneumonia, have been linked to their use. The inadvertent intravenous injection of oil, the diluent of some lipophilic anabolic steroid preparations, may damage the pulmonary capillary bed. It is unknown whether the lung injury in our patients was caused directly by the anabolic steroid, the formulation, hypersensitivity or the presence of contaminants. Injection of anabolic steroids may lead to pulmonary toxicity and requires further investigation.

87. Late Onset Dystonia Following Risperidone Overdose

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Objective: Risperidone overdose is generally associated with mild and predictable clinical effects, including sedation, tachycardia and dystonia, which are usually resolved within 24 hours of ingestion. We report the management of a case of risperidone overdose in a 28 year old woman who remained asymptomatic for almost 60 hours post-ingestion before the sudden onset of an acute dystonic reaction of the tongue and throat. *Case report:* The patient presented following the sudden onset of extremely distressing spasm and swelling of her tongue, neck and side of face, two and a half days

after an alleged overdose with 90 mg of a friend's risperidone. She was dyspnoeic and could not speak. Examination was unremarkable except for an acute dystonia of her tongue and throat, noisy breathing without true stridor, and sinus tachycardia (HR 150). Neurological examination was normal except for the dystonia. Coagulation, renal and liver function test results were within normal limits. Procyclidine was given as an intravenous bolus of 10 mg. The patient described a reduction in the swelling and spasm of her tongue and throat within 30 minutes of treatment. Serum risperidone concentration at the time of presentation was below the limit of detection for the assay and the concentration of the active metabolite, 9-OH risperidone, was 31 µg/L, which is within the normal range of 10 - 90 µg/L for patients taking risperidone therapeutically. Her heart rate settled following resolution of the dystonia and she was discharged the same day. *Conclusion:* This case report confirms that dystonic reactions can occur some days after an otherwise asymptomatic overdose of risperidone, even in the absence of elevated blood concentrations of the parent drug or its metabolite. Although dystonic reactions are not usually life-threatening, the localisation in this case of the dystonia in the mouth and throat led to severe distress that was treated effectively with procyclidine.

88. Non-Acetaminophen Drug-induced Liver Injury: Reports to a Poison Information Center

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Objective: Antimicrobials and CNS drugs are the foremost non-acetaminophen causes of drug-induced liver injury (DILI). Reports of DILI by herbal drugs are becoming more frequent.[1] Furthermore, in a retrospective analysis of medical inpatients, antibacterials, heparins, tuberculostatics and antineoplastic agents most frequently caused DILI.[2] *Methods:* In performing a retrospective analysis, we searched the database of the Poison Center (PC), Freiburg for human exposures to pharmaceuticals associated with an increase in liver function. This analysis examines the time period from 01/2000 - 09/2009. We screened our information using the German Summary of Product Characteristics (SPC) in order to identify known side effects at the time of the report to the PC. Inclusion criteria: there must be information on nature and severity of liver parameter increase as well as documented information on intake and substance. Exclusion criteria: co-medication of acetaminophen, causality assessment improbable. *Results:* Our study comprised 65 patients from 2 - 86 years (27 males and 38 females). Monointoxications prevailed (39). Drug intake in context of a suicide attempt dominated with 32 patients followed by side effects in 27 cases. Most cases of liver injury were characterized as hepatocellular (52). We found antibiotic, analgesic, antipsychotic, antiepileptic and antihypertensive drugs as the most reported drug-families. The SPC supplied with the following drugs does not contain a warning about potential liver damage: lormetazepam, prothipendyl, *Pelargonium sidoides* extracts and *Vaccinium macrocarpon*. DILI was not among the known side effects at the time of first reports of three accidental overdoses of montelukast with associated liver damage. *Conclusion:* Along with acetaminophen there are many different drugs that cause liver injury after intake of overdoses and even therapeutic doses. One competency of poison centers is to collect and compare spontaneously reported cases and reveal additional side effects of drugs after market authorization. *References:* 1. Liss G, Lewis JH. Drug-induced liver injury: what was new in 2008? Expert Opin Drug Metab Toxicol 2009; 5:843–60. 2. Wang YP, Shi B, Chen YX, et al. Drug-induced liver disease: an 8-year study of patients from one gastroenterological department. J Dig Dis 2009; 10:195–200.

89. Paediatric Toxic Incidents Related to Chemical Exposures in the Spanish Toxicosurveillance Program

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Objective: To show the profile of paediatric toxic incidents caused by chemicals in the Emergency Departments of Spanish Hospitals, as part of a program carried out by the Health Ministry and the Clinical Toxicology section of the Spanish Association of Toxicology (AETOX) over a 10-year period. *Methods:* Cases involving patients under the age of 16 years were selected from the totality of chemical incident cases reported to the Spanish Toxicosurveillance Program (TSP) in order to present their epidemiological and clinical profile and compare it with the characteristics of total chemical incidents (6012 cases) from 20 hospitals, and with the total of toxic paediatric cases in the ED of our hospital during the same 10-year period (837 cases). *Results:* From among the total chemical cases those under the age of 16 years comprised 792 (11%). The proportion of males was 54.8% and females 45.2%. 96% were household accidents. 69% of the cases involved patients under age 5 years. The main families of chemicals involved were: toxic gases (176), irritant gases (18) caustics (223), solvents (88), detergents (96) and pesticides (62). The main individual agents were: carbon monoxide (173 cases) and domestic bleach (102 cases). The route of exposure was 68% oral, 26% respiratory, 4% cutaneous, and 2% ocular. 62% of cases had had some clinical symptoms: 150 neurological, 51 respiratory, 287 digestive, 13 cutaneous and 6 cardiovascular. Some treatment was used in 527 cases: gastric decontamination in 88, cutaneous or ocular decontamination in 28, antidotes in 165 (oxygen 148, ethanol 2, methylene blue 2, atropine 4, vitamin K 4) and symptomatic in 302 cases. There were no fatal cases recorded, nor relevant sequelae. *Conclusion:* The main differences from the overall chemical cases were related to sex distribution (no difference in the total group), the absence of intentional cases in the paediatric population, and the chemical agents involved - with fewer cases of the most dangerous products, such as hydrochloric acid and methanol in the paediatric population, and a consequently better prognosis. The main differences within the total paediatric toxic cases were determined by the presence of ethanol and different medicines causing a peak of intentional poisoning in the 13–15 age group.

90. National Poison Data System: Methadone Exposures 2000–2008

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Objective: In response to reports of increasing morbidity and mortality related to methadone HCl 40-mg tablets, the United States Drug Enforcement Administration (DEA) issued an advisory in late 2007. As of 1 January 2008, manufacturers of methadone 40-mg tablets voluntarily agreed to limit their wholesale distribution to DEA-registered opioid detoxification and maintenance facilities and hospitals. Retail pharmacies and other healthcare providers would not be able to purchase methadone 40-mg tablets. We studied all methadone and 40-mg methadone drug identification and exposure data from the National Poison Data System (NPDS) for 2000 - 2008 to evaluate the impact of this intervention. *Methods:* 40-mg methadone was then available in 10 products from 6 manufacturers. NPDS database was queried for human exposure case and drug identification case data on these products for the years 2000–2008. Human exposures, deaths, death by indirect report and drug identification data were examined by linear and log-linear regressions to examine temporal patterns and rate of growth as indicated by doubling time (DT). *Results:* All methadone exposures per year 2000–2006 had a DT [95% CI] of 3.51 [2.71, 4.98] years. 40-mg exposures DT was 1.52 [1.19, 2.12] years with the 2008 value lying well below the 95% CI. All methadone deaths per year had a DT of 3.08 [2.26, 4.82] years and 40 mg deaths DT was 1.85 [1.23, 3.73] years. All methadone drug ID calls per year 2000–2007 had a DT of 2.06 [1.71, 2.57] years and 40-mg drug ID calls DT was 1.91 [1.53, 2.54] years with the 2008 value lying well below the 95% CI. All methadone drug ID calls per month suggested a distinct change in calls beginning after July 2006, initially increasing and then decreasing. 40 mg drug ID calls fell below the 95% CI beginning October 2007. *Conclusion:* Recent temporal patterns show changes which could reflect the DEA's 40-mg intervention in 2008. NPDS data shows 40-mg methadone exposures decreased, deaths decreased, and Drug ID Calls increased and then decreased and signaled a response. NPDS provides national real-time data with the potential to assess regulatory or enforcement interventions.

91. National Poison Data System: Enhancing Public Health Surveillance by Delivering Poison Center Call Information Using Secure Web Services

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Introduction: Biosurveillance is the systematic process of data collection and analysis for timely detection and characterization of disease outbreaks in humans and animals. Biosurveillance systems use a variety of clinical and non-clinical data (e.g. poison center reports, emergency department chief complaints). Most systems employ specialized data collection mechanisms and databases, and use outbreak detection algorithms and user interfaces to analyze and visualize information. The National Poison Data System (NPDS) is a biosurveillance system for the collection and analysis of poisoning exposures for the United States. Since its inception, NPDS has received requests from public health and other agencies to integrate NPDS data with their biosurveillance information. In 2008, we began sharing NPDS data by building an NPDS Web Service to distribute aggregated counts of NPDS data. Subsequently, in 2009 we built an additional web service to provide detailed case data. *Methods:* The NPDS Web Services use standard Simple Object Access Protocol (SOAP) and the .NET programming language. External systems access NPDS Web Services using the programming language of their choice or our open source client. We encrypt all communications using Secure Socket Layer (SSL) protocol and authenticate each data request using a username and password. Users are restricted from accessing data outside of their jurisdiction using role-based authorization. *Results:* Since the original NPDS Web Service went online in September 2008, 72 users have generated a total of 9056 queries: 6089 Clinical Effect (signs and symptoms); 2329 Total Call Volume; 606 Human Exposure requests. The new web service implemented in October 2009, has received 32 Case Detail requests. *Conclusion:* NPDS web services provide a cost effective approach to sharing and maintaining data across organizations and jurisdictions, and illustrates a federated approach to biosurveillance. Because we utilized standard web service technology, NPDS poison center data is always current. Since the data is available as a service, we have obviated the need to duplicate the data in the local system reducing expenditures in hardware and software. These characteristics expedite outbreak detection with timelier data, as well as reduce hardware/software, and labor costs to maintain redundant data and customized interfaces.

92. Lyell's Disease - the Most Severe Adverse Drug Reaction and Difficult to Treat (Case Series)

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Objective: Lyell disease (toxic epidermal necrolysis) is a severe acute skin disorder, described for the first time in 1956 by Alan Lyell. This condition is most often drug induced (NSAIDs, barbiturates, some antibiotics, etc) and is characterized by generalized erythema, confluent macules with subsequent generalized epidermal sloughing, mucous membrane involvement, persistent fevers, positive Nikolsky sign. Although rare (average incidence of toxic epidermal necrolysis is 0.5–1.4 cases per million population per year) this condition has a bad prognosis - with estimated mortality rate of 10–70%, depending on the quality of care and the rapidity with which treatment is initiated. The pathophysiology of toxic epidermal necrolysis has not yet been fully elucidated; however, various theories have received wide acceptance. Toxic epidermal necrolysis is believed to be an immune-related cytotoxic reaction aimed at destroying keratinocytes that express a foreign antigen. *Case series:* We present a case series of 150 patients with Lyell's disease treated over the period 1978 - 2008. The age of the patients varied from 19 months to 80 years (28 children and 122 adults). The survival rate observed was 60% throughout the whole period. *Conclusion:* Lyell's disease is a life threatening severe disorder requiring timely diagnosis and aggressive treatment. Special attention is paid to the standard treatment protocol at the Toxicology Clinic, MHATEM "Pirogov" as it is well known that mortality rate is highly dependent on the aggressiveness of the treatment strategy, quality of care and rapidity with which treatment is initiated.

93. Enquiries to the UK National Poisons Information Service Regarding Dextromethorphan Toxicity

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Objective: Dextromethorphan is a readily accessible antitussive agent. Recreational abuse has been associated with dissociative effects, and deaths have been reported after ingestion of very large doses.[1,2] This study examined the clinical features associated with dextromethorphan ingestion in the United Kingdom. *Methods:* The National Poisons Information Service is commissioned by the Health Protection Agency to provide clinical advice on the management of poisoned patients in the United Kingdom. Enquiries concerning dextromethorphan were examined retrospectively. *Results:* Data were available between 2004 to 2007. There were data concerning 354 patients with median age 7 years (95% CI 4 to 14 years) of whom 194 were female (55.0%). Cases involved accidental ingestion in 261 (73.9%), deliberate overdose in 87 (24.6%), and adverse effects of therapeutic dose in 5 (1.4%). Median dose was 45 mg (range 3 to 2750 mg). Commonest co-ingested agents were paracetamol in 147 (41.6%), promethazine in 132 (37.4%), diphenhydramine in 73 (20.7%), pseudoephedrine in 67 (19.0%), triprolidine in 53 (15.0%), and menthol in 32 (9.1%). There were no symptoms or signs of toxicity in 257 patients (72.8%). The dose was higher in patients with symptoms; 120 mg (IQR 50 to 225 mg) versus 30 mg (IQR 8 to 90 mg), $p<0.0001$ by Mann Whitney test. Dextromethorphan dose was predictive of toxicity; receiver operating characteristic AUC 72.5% (95% CI 67.1 to 77.4%). Clinical features were drowsiness in 50 (14.2%), minor haemodynamic effects in 14 (4.0%), nausea or vomiting in 13 (3.7%), dizziness and ataxia in 10 (2.8%), agitation in 7 (2.0%), non-specific abdominal pain in 4 (1.1%), mydriasis in 3 (0.8%), dry mouth in 3 (0.8%), blurred vision in 2 (0.6%), headache in 2 (0.6%), and tremor in 1 (0.3%). None had features of severe poisoning. *Conclusion:* Dextromethorphan enquiries to the National Poisons Information Service often concern accidental exposures in children. The majority of patients had no clinical features or only minor symptoms. *References:* 1. Logan BK, Goldfogel G, Hamilton R, et al. Five deaths resulting from abuse of dextromethorphan sold over the Internet. J Anal Toxicol 2009; 33:99–103. 2. Romanelli F, Smith KM. Dextromethorphan abuse: clinical effects and management. J Am Pharm Assoc 2009; 49:e20-e25.

94. Electronic Product Notifications of Industry to BfR: Development of a Uniform Standardized Data Set for Information of the German Poison Control Centres Under Art. 45 Clp Regulation

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Objective: Since 20 January 2009, the CLP Regulation (EC) No. 1272/2008 has been in effect in the EU. Article 45 stipulates compulsory reporting of formulations of mixtures by the industry for emergency health services. Having to collect such information in Germany, BfR is developing a uniform standardized electronic data set for product data supplied by companies. *Methods:* Since 2007, notification of formulations of detergents and cleaning agents has been performed by file transfer in XML format. This procedure was developed by BfR and has been adopted by industry very well. It is currently being refined by BfR to ensure that data on all notifiable products and data reported on a voluntary basis can be transmitted in XML format. After completion and testing of the prototype at BfR in spring 2010, it is envisaged that the procedure will be tested in practice by a major enterprise (Henkel, Düsseldorf). The BfR database is being adapted to the new requirements of the CLP Regulation on e.g. labelling. All important data, including clear identifiers (e.g. product identification element) will be exchanged in the new format. *Results:* In the 2000–2006 period, a harmonized joint PCC/BfR classification system by product application groups was developed under the BMU TDI research project, in cooperation with the Association of Clinical Toxicology. This system is being adopted by the BfR database. Classification of products at BfR and subsequent communication to PCCs by means of XML exchange format will facilitate a harmonized evaluation of cases of poisoning. The data acquisition system at BfR and the exchange format are adapted to the new requirements of the CLP Regulation and subjected to practical testing. To warrant a secure data transfer, a dedicated portal for receiving formulation data has been established. For clear product identification, a symbol has been created and fixed in a CEN standard. *Conclusion:* A universal electronic notification procedure for industry will enable BfR to considerably increase the number of product notifications received, processed and communicated to German PCCs. Under risk minimization aspects, a new product classification system will also allow evaluation on the basis of the BfR product data sets.

95. Adult Metformin Ingestions Reported to the Danish Poison Information Centre

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Objective: The biguanide metformin has recently been promoted as a first line treatment in type 2 diabetes.[1] National statistics show that metformin sales have increased by 36% in defined daily dose (DDD) over a period of just 2 years.[2] Metformin is known to cause potentially fatal metabolic lactic acidosis in both overdose and therapeutic use, which is observed in 3 cases per 100,000 patient-years of therapeutic use.[3] In Denmark, adverse effects are reported to the Danish Medicines Agency whereas overdoses are registered by the Danish Poison Information Centre (DPIC). Limited information exists about the pattern of adult metformin ingestions reported to DPIC. *Methods:* Twelve adult cases of metformin ingestions registered by DPIC over a 3-year period from August 2006 to November 2009 were reviewed. Patient age, sex, serum-pH, and serum-lactate and creatinine concentration were registered. When available, ingested metformin dose, suspected attempted suicide, coingestions, and whether patients received haemodialysis were analyzed. *Results:* There were 5 women (42%) and 7 men (58%). Mean age was 45 years (range 20–70 years). The mean reported dose was 1,913 mg (range 550–50,000 mg). In 6 out of 12 cases, ≥ 1 co-ingestions were involved, primarily antipsychotic drugs (25%) and NSAIDs (25%). Suicide attempts 10/12 (83%) and 5/12 (42%) had a concomitant abuse of alcohol. The most commonly reported adverse clinical effects were vomiting, nausea, gastrointestinal pain and headache. Mean pH was 7.25 (range 6.99–7.38), and highest serum-lactate registered was 23 mmol/L. In 4 cases, serum-creatinine was > 282.5 mmol/L. In total 8/12 (67%) were referred to the ICU - 4 of whom (50%) were started on haemodialysis. All patients survived. *Conclusion:* Metformin ingestions registered by DPIC require intensive therapeutic care in the majority of cases, but mortality is low. *References:* 1. Salpeter S, Greyber E, Pasternak G, et al. Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus: systematic review and meta-analysis. Cochrane Database Syst Rev 2006; 1:CD002967. 2. Danish Medicines Agency, Consumption and Statistics, Last updated - 12.11.2009. 3. Forrester MB. Adult metformin ingestions reported to Texas poison control centres, 2000–2006. Hum Exp Toxicol 2008; 27:575–83.

96. Retrospective Review of Ephedrine Exposures. An Observational Case Series

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Objective: Ephedrine is a sympathomimetic used in supplements claiming to produce effects such as euphoria, increased sexual sensation, and weight loss. The use of these products has been associated with a number of serious side effects such as cardiac arrhythmia, seizures, and possibly death.[1] Although illegal in Denmark, these products are easily available through Internet sale. The objective is to conduct a risk assessment of ephedrine containing products. *Case series:* We conducted a retrospective review of all telephone inquiries involving ephedrine registered in our database in the period August 2006 to October 2009. We identified 65 cases involving products containing ephedrine. Forty-two (64%) of our study subjects were female. Three subjects (5%) were small children (age 1 and 2 years old), who accidentally ingested their parents' medication. Eight (12%) cases were teenagers (mean age 16, range 14 to 17). All ingestions were intentional, three of them suicidal. Fifty-one (78%) were adults (mean age 28, range 18 to 54). Also in this group all intakes were intentional, and seventeen were suicidal. The intentional intake without suicidal attempts ranged from 24 to 3000 mg (mean dosage 413 mg). The dosage in suicidal attempts ranged from 24 to 16,440 mg (mean dosage 1593 mg). The accidentally ingested dosage among the children could not be specified. Fifty-seven subjects (87%) did experience adverse effects. Cardiovascular effects were the most common [tachycardia (43%), chest pain (7%), hypertension (5%) palpitations (5%)]. Gastrointestinal symptoms were reported in 14% of the cases [abdominal pain (5%), vomiting (11%)]. Eleven per cent of the subjects experienced restlessness and/or agitation. None of the cases was fatal, but 3 (4.6%) had serious adverse reactions (unconsciousness, acidosis and convulsion) that required intensive treatment. The ingested dose did not appear to be correlated to the observed clinical effects. *Conclusion:* Although no fatalities were registered, our case series supports the proposal that ephedrine-containing supplements pose a considerable risk of adverse reactions, and uncontrolled use must be considered dangerous. The lack of correlation

between dosage and severity of symptoms indicates that individual disposition plays a considerable role in the response to ephedrine. *Reference:* 1. http://www.dkma.dk, 11-11-2009.

97. Severe Mercury-Poisoning of a Child and Involvement of the Whole Family

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Objective: Elemental mercury is well absorbed via inhalation with the risk of damage to the central and peripheral nervous system after chronic exposure. We report a case of mercury-poisoning of a child with severe injury to the peripheral nerves. The involvement of the other family members is documented, as well. *Case report:* A 13-year-old boy found a box containing metallic mercury in an old factory and played with it at home for many days in November 2008. During the next few weeks he developed a progressive leg-emphasized frailty, hyporeflexia and paresthesiae of the extremities. In addition, he presented nausea, headache, and psychological signs in terms of mood and behaviour. Signs of axonal neuropathy were seen in electroneuromyography in February 2009. The initial mercury-level in urine was 360 µg/L. During the DMPS treatment for several months the mercury level in urine fell into normal range, but the severe neurological symptoms persisted nearly unchanged. Within 6 months he was able to write again. One 11-year-old brother with a mercury level in urine of 327 µg/L showed symptoms like pallor, dizziness, nausea, and headache. The other 15-year-old brother with a mercury level in urine of 270 µg/L had no symptoms. The siblings and the father, who had only mild symptoms and a mercury urine level of 174 µg/L, were treated with DMPS, as well. *Conclusion:* The child developed a severe secondary peripheral neuropathy, despite mercury urine levels in the lower toxic range. DMPS-treatment reduced the mercury urine level to a normal range during 10 weeks, but the neurological symptoms improved slowly over several months. Apparently, the storage of the heavy metal in the nervous system was complete at the time of diagnosis and it could not be mobilised sufficiently by the antidote. In contrast to the brothers, there was no increase of the mercury urine level at the beginning of the medication suggesting interindividual differences of mercury storage or metabolism.[1] *References:* 1. Gundacker C, Wittmann KJ, Kukuckova M, et al. Genetic background of lead and mercury metabolism in a group of medical students in Austria. Environ Res 2009; 109:786–96.

98. A Five-Year Retrospective Study of Toxic Coma in a Pediatric Emergency Department

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Objective: To study the prevalence of coma due to acute poisoning in children examined in a Pediatric Emergency Department. *Methods:* We have analyzed all the children who attended the Emergency Department in our hospital during a five year period, taking into consideration the following: consciousness status assessed by Glasgow Scale, type of poisoning that resulted in coma, distribution by: age, gender and reason for presentation (accidental or intentional). *Results:* Between November 1st and October 30th 342 children with coma were registered, i.e. 0.5% out of the total number of 68,326 examined in the Emergency Department. Toxic coma was diagnosed in 220 cases representing 64% of comatose patients. The main poisons leading to coma were: ethanol: 63 patients (29%) and multiple drug poisoning: 46 cases (21%). These were followed by: benzodiazepines: 15 patients (7%), antidepressants: 11 cases (5%), Dentocalmin (lidocaine, menthol and phenol): 11 (5%), barbiturates: 9 (4%), pesticides: 5 cases (2%), hydrocarbons 3 (1.5%), carbon monoxide: 2 (1%), heroin 1 case (0.5%). In 20% (44 cases) of cases with toxic coma the etiology was unknown at the time of presentation, being established later in the Toxicology Department. According to the reason for presentation we noted 155 cases with intentional poisoning (70%) and 72 with accidental poisoning (30%). *Conclusion:* Despite the prevalence of toxic coma in the totality of emergencies not being very high, it remains one of the most severe life-threatening situations in the pediatric pathology. Toxic etiology represents the main cause of coma in children. Consequently, when faced with a child with sudden coma we must always think about poisoning. *References:* 1. Shannon MW. A General Approach to Poisoning. In: Shannon M, Borron S, Burns M, eds. Haddad and Winchester's Clinical Management of Poisoning and Drug Overdosage, 4th ed. Philadelphia, USA: Saunders Elsevier Inc., 2007:13–30.

99. Do People Use Over-the-Counter Drugs Safely? An Analysis of 409 Cases Of Domestic Medication Errors with Acetaminophen Reported from the Poison Control Centre of Milan, Italy

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Objective: A review of data collected by the Poison Control Centre of Milan shows that acetaminophen is the drug most frequently involved in domestic medication errors, an underestimated cause of accidental poisonings. The overdose of this drug, frequently caused by a wrong use, is characterised by serious, potentially fatal hepatic damage. As in Italy acetaminophen is sold without medical prescription and it is widely used as an antipyretic in children, it seems extremely important to analyze the frequency and circumstances of these unintentional medication errors. *Methods:* A review of calls concerning domestic medication errors collected between 01/01 and 31/12/2005 by PCC of Milan was analysed to point out all the cases related to acetaminophen misuse. Among these, 100 cases involving children were selected for a telephone interview to find out how the incident occurred. *Results:* Acetaminophen was the drug most frequently involved among 3193 cases of medication errors collected, accounting for 13% (n = 409) of the total. 1309 patients (41%) were admitted to the hospital and 105 (3.3%) received antidotal treatment with N-acetylcysteine (NAC). Most of the patients (63.3%; n = 2021) were children aged 0–14 years. The interview revealed that the mistake was mostly made by one of the parents (77%) or by another relative (18%). Generally the drug had been already used in the past (89%) and in this occurrence it was administered without medical prescription (95%), based on previous personal experience (91%). Most of the interviewees (75%) were unaware of the harm associated with acetaminophen overdose. Most of those who knew about the potential hepatotoxicity of the drug said they learned about this risk only after the incident (77%). *Conclusion:* Acetaminophen misuse seems mainly related to people's lack of awareness about the toxic effects of acetaminophen overdose and the erroneous belief of using the drug safely even without medical advice. In general terms, this risk appears highly relevant when drugs freely available for paediatric medication are improperly used by parents. Domestic medication errors should be better investigated as they are an underestimated, preventable health risk to the population.

100. Risk of Adverse Events Related to Flumazenil in the Treatment of Patients with Suspected Benzodiazepine Overdose. A Meta-analysis

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Objective: The purpose of this meta-analysis is to estimate the risk of adverse events (AE) associated with the use of flumazenil in patients with impaired consciousness due to suspected benzodiazepine overdose. *Methods:* Randomised controlled studies including patients with impaired consciousness due to suspected benzodiazepine overdose (pure or mixed) and treated with flumazenil or placebo were considered for this analysis. We performed a systematic literature search using the databases PubMed, EMBASE and Cochrane Library and searching reference lists from included studies and previously published reviews. Numbers of AEs were registered from each study and a pooled relative risk was calculated using a fixed effect model. Potential result heterogeneity was evaluated visually by examination of the Forest plot and chi square-test. The overall number of AEs and the number of serious AEs were analysed separately. Serious AEs were defined as AEs that are life threatening, prolonging hospitalisation or causing permanent disability. The incidence of AEs was estimated from the difference between AEs in the flumazenil and the placebo group. *Results:* Twelve studies (including 955 participants) were included in the analysis. Nine studies confirmed the inclusion of mixed intoxications by blood concentration measures. None of them reported fatalities. Serious AEs registered were: hypotension, ventricular arrhythmia and convulsions. Other AEs registered were: restlessness, agitation, crying, vomiting, nausea, headache, sweating, and injection site pain. The overall risk of experiencing an AE was significantly higher in the flumazenil treated group (Relative Risk 4.07, CI 95% 2.80, 5.91). Although serious AEs only occurred in flumazenil treated patients, the overall risk of serious AEs was not significantly different between the flumazenil and placebo group (Relative Risk 3.50, CI95% 0.84,14.62). The overall incidence of AEs and serious AEs was 0.19 and 0.01, respectively. *Conclusion:* Flumazenil treatment in patients with impaired consciousness due to suspected benzodiazepine overdose is associated with a significant risk of AEs. Most of these are mild and should not indicate any treatment-restrictions. However, the current evidence does not allow estimating the relative risk of serious AEs precisely enough to support the routine use of flumazenil. This treatment should therefore only be used after careful consideration.

101. Neuraminidase Inhibitor Overdoses: The Other Side of Pandemic Influenza

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Objective: As a result of the global influenza pandemic, use of antiviral drugs has increased. Unfortunately, there are very little published data regarding overdose with either of the two available oral neuraminidase inhibitors (NIs); oseltamivir and zanamivir. This study evaluates outcomes of unintentional therapeutic errors (UTEs) with NIs. *Methods:* Adverse events from NI UTEs were collected prospectively on a standardized data instrument. A retrospective review was performed of all NI cases from January to November 2009. Only single substance UTEs with known doses were included for final analysis. *Results:* A total of 30 NI cases were initially collected; 18 involved children and 12 involved adults. 17/18 children had unintentional therapeutic errors (UTE), the other was a drug interaction with ethanol. Among the 12 adults, there were 7 UTEs. The 5 excluded adult cases comprised; one polydrug suicide, and four possible adverse drug reactions at therapeutic dosing. Among children, the ages ranged from 15 months to 16 years old. The UTEs ranged from double the dose to eight times the therapeutic dose. A total of sixteen patients had acute dosing UTEs and four had chronic UTEs. Five patients developed symptoms; a 16 year old who vomited two hours after a double dose (150 mg) oseltamivir; a 9 year-old who received a double dose (150 mg) oseltamivir had vomiting in the morning and then vomited again after the dose; a 7 year-old who got 30 mL (12 mg/mL) oseltamivir instead of 5 mL complained of abdominal pain; a 5 year-old who got 20 mL (12 mg/mL) oseltamivir vomited twice and was febrile; and a 5 year-old who received 15 mL instead of 4 mL (12 mg/mL) oseltamivir suspension

and vomited. For the adult cases, two were acute double dosing errors and two where chronic. One patient, taking 75 mg oseltamivir BID for two days developed a rash and swelling on both hands and feet. *Conclusion:* In this series of 24 cases, unintentional therapeutic errors with neuraminidase inhibitors appear to produce minimal transient toxicity. Similar gastrointestinal symptoms should be expected following intentional ingestions of doses up to a standard course of therapy (750 mg in an adult).

102. Neurotoxicity Due to 3,4-Diaminopyridine Treated Successfully with Lorazepam

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Objective: Previous reports of toxicity due to 3,4-diaminopyridine (DAP) have only described mild paresthesias and abdominal pain. However, no reports of acute overdose exist in the literature. We describe a case of unintentional overdose of 3,4-diaminopyridine presenting with severe abdominal pain, back pain, diaphoresis and painful ascending paresthesias of all 4 extremities. *Case report:* A 57-year-old woman with a past medical history of Lambert Eaton myasthenic syndrome (LEMS) presented to the emergency department with unintentional overdose of DAP just prior to arrival. She had recently been instructed to increase her prescribed dose from 10 mg to 15 mg 3 times per day, but had taken 20 mg. The patient immediately developed severe abdominal and back pain, diaphoresis, and painful paresthesias of all 4 extremities. Vital signs on arrival were: HR 74 bpm, BP 139/74 mmHg, RR 22 bpm, temperature 36.8 °C, and 100% oxygen saturation on room air. Electrocardiogram revealed a sinus rhythm at 65 bpm with a QTc of 436 ms. Physical examination revealed a patient in moderate distress with diaphoresis, diffuse tenderness of her abdomen and thoracolumbar paravertebral musculature. The remaining physical examination was normal. The patient was treated with lorazepam 1 mg intravenously with resolution of all symptoms within 2 minutes. Laboratory values including chemistry, creatine phosphokinase, and liver function tests were all normal. The patient did not experience any increased weakness, remained asymptomatic for 24 hours and was reinitiated on her original medication regimen the following day. *Conclusion:* DAP has not been approved in the United States for use in LEMS despite multiple studies confirming its efficacy. DAP has been preferred over aminopyridine because of less expected neurotoxicity via blood brain barrier permeability. This case demonstrates that DAP also has a very narrow therapeutic index despite its utility. Prior reviews have mentioned the potential benefit of phenytoin coadministration in preventing seizures and neurologic toxicity; however, in our case, all adverse reactions were immediately and successfully treated with a single dose of lorazepam.

103. Naltrexone Interaction with Opioid Induced Withdrawal Syndrome Follows a Binary Pattern of Severity in Contrast to Post Opioid Overdose

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Objective: Opioid overdose is common.[1] Overdose with short half life opioids usually leads to withdrawal symptoms in the day following admission. Naltrexone, an opioid antagonist, can also cause withdrawal symptoms in dependent subjects.[2] This study aimed at comparing the frequency of withdrawal manifestations in opioid naltrexone interaction and post overdose. *Methods:* All consenting subjects with opioid naltrexone interaction (N) and a quarter of diamorphine overdose subjects (O) (systematic selection) from November 2008 to April 2009 were studied prospectively, as a part of a wide randomised clinical trial. Ethical approval was obtained (MUMS-6367). N subjects received fluids and diazepam. O cases received fluids and naloxone if needed. *Results:* 25 N and 21 O subjects were studied. On admission, pain, agitation, sweating, piloerection, muscle cramp, nasal congestion, yawning, tremor, nausea, muscular and bone pain, pupil size and respiratory rate were significantly different (P<0.001 for all). Craving, pulse rate, systolic and diastolic blood pressures and temperature were not different. Twenty-four hours after exposure insomnia (0.004), nausea (0.032), pupil size (0.006) tremor (0.035) and respiratory rate (0.037) were still significantly different. Other findings were similar. Descriptively, severity of these variables was gradually increasing in the first 24 hours in overdosed subjects. Naltrexone cases, however, followed a binary pattern in severity of some of these variables including pain, muscle cramp, sweating, tremor, piloerection, respiratory rate and pupil size in this period. *Conclusion:* Clinical manifestation of withdrawal symptoms/signs post overdose and after naltrexone interaction with opioids is different. While naltrexone induces a binary pattern of increased severity of findings, overdose cases experience constant intensification of symptoms. O and N cases are more different on admission than 24 hours later. Some differences might be due to diazepam administration. *References:* 1. Hall AJ, Logan JE, Toblin RL, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. JAMA 2008; 300:2613–20. 2. Singh SM, Sharma B. Unintentional rapid opioid detoxification: case report. Psychiatr Danub 2009; 21:65–7.

104. Causality Assessment For Pediatric Drug Induced Liver Injury Using Poison Center Data

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Objective: United States Poison Centers receive over 1 million calls reporting pediatric exposures each year. Poison center data has been used as a post-marketing signal for adverse medication effects, including liver injury. The purpose of this study was to evaluate the performance of a structured causality assessment using poison center data. We selected acetaminophen as our target medication because it is common and cases of liver injury can be readily categorized as due to acetaminophen from the information collected by poison centers. *Methods:* Ten pediatric cases (age <6 years) reported to US Poison Centers which described liver injury and acetaminophen exposure were selected. Four toxicologists independently reviewed the cases using the RUCAM assessment tool. After the initial scoring, the reviewers were asked to rate the certainty that the drug event was due to acetaminophen using the WHO-UMC scale and a gestalt score of 0–100% chance of being caused by acetaminophen. RUCAM agreement between reviewers for a case was defined as all reviewers within 2 points for the overall score. *Results:* Using the RUCAM system, 3 or 4 reviewers rated 8 cases as possibly related and 2 cases were rated as not related to acetaminophen; no cases were rated as probable or certainly related to acetaminophen. All reviewers were within 2 points for 8/10 cases. Using the WHO scale, 8 cases were rated as probable and 2 were rated as certain by 3 or 4 reviewers. Using the Gestalt scale all cases were rated as at least an 80% chance of being acetaminophen induced. *Conclusion:* The RUCAM score had fair agreement but appears to underestimate the probability of causality for identifying pediatric cases of liver injury due to acetaminophen using poison center data. Our results are limited to pediatric exposure to acetaminophen, but it is likely that exposures in adults and to other substances would have included similar information. The performance of these tools could be improved by better data collection at poison centers nationwide. Alternatively, a modified scale could be developed for poison center data.

105. Digoxin Antibody Use in Elderly Patients in Lille Hospital

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Objective: Evolution of elderly patients treated with digoxin antibodies. *Methods:* A retrospective analysis of digitalis poisoning cases occurring in subjects aged more than 70 years and hospitalized in Lille between 2003 to 2008 and treated with digoxin antibodies by the Poison centre of Lille. To consider initial and total severity, the criteria used were those described by Persson and colleagues.[1] *Results:* 26 patients were hospitalized and treated with Fab. The average age was 81.4 ± 6.7 years (range: 71–97 years). Eighty-one per cent were women (sex ratio: 0.23). The cause was a chronic overdose in 92% and for 8% a suicidal act. Poisoning occurred mainly at home (92%). All the patients were receiving digoxin treatment for a chronic cardiac condition. Fifty-eight per cent of the patients arrived by ambulance. All the patients were symptomatic at the time of their initial health care management. Clinical severity was considered as being moderate in 15 patients (57.7%), severe in 10 patients (38.5%) and minor in 1 patient (3.8%). The electrocardiogram showed conduction disturbances in 14 patients, an arrhythmia in 19 patients and bradycardia in 17 patients. The average digoxin serum level was 6.64 µg/mL ± 4.77 (min 2.6-max 22.9). The average serum potassium was 5.9 ± 1.2 (range 3.4- 8.7). Twenty-five of the patients received digoxin antibodies for curative and prophylactic treatment, according to the protocol used by F. Lapostolle et al.[2] The number of vials received was on average 4.8 (range 1–12), calculated in Digidot vials. Outcome was good for 19 patients (73%) and fatal for 7 patients (27%); hospitalization averaged 7 days (range 1–90 days). There were no complications due to treatment with Fab. *Discussion:* This series shows that serious intoxications in elderly subjects requiring Fab occur primarily at home and involve chronic accumulation in therapeutic use. The health care management is onerous with an average duration of 7 days hospitalization in spite of the use of Fab. Mortality remains very high even if it has decreased considerably since the introduction of Fab (50% without Fab from the literature). It should be noticed however that it remains much higher than in the general population (6%). This confirms the vulnerability of the older subjects to digoxin poisoning. *Conclusion:* Managing elderly patients is often complex because of the polypathology and polymedication. Digoxin poisoning remains serious and even fatal in spite of treatment. A possible research study would be the time to diagnosis and health care management of elderly subjects. *References:* 1. Persson HE, Sjöberg GK, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol 1998; 36:205–13. 2. Lapostolle F, Borron SW, Verdier C, et al. Assessment of digoxin antibody use in patients with elevated serum digoxin following chronic or acute exposure. Intensive Care Med 2008; 34:1448–53.

106. High-Fidelity Simulated Toxidromes in Medical Student Education

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Objective: In an effort to familiarize medical students with frequently encountered toxic exposures, a curriculum was designed to simulate a poisoned patient. The simulation required the students to recognize, diagnose and treat the toxidromes represented on a mannequin. *Methods:* A medical toxicology curriculum was created for fourth year medical students rotating through the Emergency Department which included a classroom lecture and high-fidelity simulation cases. The cases were based around the cholinergic, anticholinergic, sympathomimetic, opioid and ethanol withdrawal toxidromes. Students were presented with a verbal scenario, and then had to proceed with a history and physical examination of the simulated patient. The students were required to act on the history and physical exam findings, as well as verbalize placement of intravenous access, initiation and dosing of pharmacotherapy, interpretation of cardiac rhythms, and modify patient management based on a response to the treatments given. The mannequin is also equipped with the ability to simulate changes in

pupil size, presence or absence of diaphoresis, seizures, respond to intravenous access, pharmacotherapy, endotracheal intubation, transdermal pacemaker, and defibrillation. The student can assess the cardiac rhythm, heart rate, blood pressure, respiratory rate, pulse oximetry, and temperature on a monitor linked to the mannequin. It is also pre-programmed to respond appropriately to correct interventions and clinically decompensate in response to incorrect diagnosis or intervention. As an initial evaluation of whether or not this curriculum improved toxicology knowledge, we evaluated subjective student reviews of the simulation curriculum on a five point Likert scale where "1" was uninformative, "3" was informative and "5" was inspirational. *Results:* Overall, 72 fourth year medical students rotated through our department between July of 2008 and October of 2009. The medical students' mean rating for this curriculum was 4.4 on a Likert scale. *Conclusion:* High-fidelity simulation provides an interactive approach to learning clinical toxicology. The medical students rated this as an affective teaching modality.

107. The Utilization of Pre-Hospital Advanced Life Support for Toxic Ingestions

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Objective: Advanced Life Support ("ALS") is requested frequently for patients with suspected drug overdose or ingestion, but its utility has not been proven. Anecdotally, many of these patients are simply observed pre-hospitally and in the emergency department ("ED"), so ALS resources may be applied more efficiently with other types of patients. We sought to determine what percent of ALS calls dispatched as drug overdose or toxic ingestion, receive acute interventions in the field. *Methods:* We retrospectively reviewed the pre-hospital records of all patients for which ALS was dispatched for "Ingestion/Poisoning" or "Overdose" over a 30 month period in a suburban, two-tiered EMS system. Prehospital charts were reviewed and pre-hospital interventions were recorded. We defined acute interventions as establishing IV access, administration of IV medications, and establishing a definitive airway. Percentages and 95% confidence intervals ("CI") were calculated to describe the proportion of patients receiving these interventions. *Results:* Out of over 41,804 paramedic dispatches, 673 (1.6%) were dispatched as "Ingestion/Poisoning" or "Overdose." Of those patients, ALS was cancelled on 16% (CI:13–18). 51% (CI:47–55) had an IV established prehospitally. Fourteen per cent (CI:11–17) received any medication, with the majority of these being naloxone. One per cent (CI:1–2) were intubated in the prehospital setting. *Conclusion:* Of all ALS dispatches for "Ingestion" and "Overdose" in our suburban EMS system, the overwhelming majority of patients receive no emergent treatment en route to the hospital. More focused dispatching of these calls may be appropriate to conserve diminishing EMS resources.

108. Pandemic Flu Increases Risk of Poisonings in Children

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Objective: In April 2009, a new influenza strain hit the population in Mexico. Soon thereafter the WHO declared this new flu strain H1N1 pandemic. As a consequence, the Norwegian Government has given advice on how to prevent the spread of the influenza infection. This includes promoting hand hygiene by alcohol-based hand disinfectants. Supplies became available in homes, day-care centres, schools and workplaces. As a result, these hand disinfectants have become more accessible for children. Has this had an impact on the number of poisonings in children? *Methods:* The National Poisons Information Centre (PIC) database was retrospectively searched for cases involving children aged 0–9 years with an alcohol-based disinfectant exposure. These cases were analyzed for their exposure characteristics and risk assessment. The data was correlated with the time schedule of the influenza outbreak and governmental advice. *Results:* There has been a huge increase of calls to the PIC concerning possible poisonings from disinfectants. During the months of June/July 2009, advice regarding use of alcohol-based hand disinfectants was given by the Government. The number of inquiries concerning exposures of disinfectants in children below ten years increased 4-fold from July to August 2009. The number of inquiries was steady from August to September 2009. By the time the influenza infection started to spread in the population and disinfectant advice was intensified, the number had increased another 1.6-fold. In total, the number of enquiries concerning children below ten years exposed to alcohol-based hand disinfectants increased 8-fold from July to November 2009. Most of the exposures (70%) were oral. However, no increase in the incidence of severe poisonings was observed in the period. The amount ingested was typically from a few drops to a mouthful, and too small to cause any severe poisonings. *Conclusion:* Increased accessibility to alcohol-based hand disinfectants has led to an increase in accidental exposures in children, with the inherent risk of poisoning.

109. Prevalence of Hepatitis B Virus and HIV in IV Drug Users in Tehran

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Objective: Injection drug use has been the major growth route of drug abuse in Iran in the past decade and it has been responsible for the transmission of HIV virus in more than two third of cases.[1] The aim of the present study was to determine the prevalence of HIV and hepatitis B in a group of IDU (IV drug users) cadavers and to compare the results to a group of cadavers in the normal population. *Methods:* In a case-control study the blood samples of the cadavers of 400 randomly chosen IDUs (IV drug users) and 400 other cadavers as control group were checked for HBS antigen and Anti HIV antibody in the Forensic Medicine Center of Tehran. The prevalence of HIV and HBV infection was compared in the two groups according to their demographic characteristics. *Results:* The number of HIV and HBV positive cadavers was significantly higher in the IDU (IV drug users) group than the controls (6.25% vs 0.5%, P<0.0001, 27.5% vs 3%, P<0.0001). The risk of being infected by the HIV virus was 13.27 times greater in the IDU (IV drug users) group and the risk of HBV infection was 12.26 times greater in this group as compared to the control group. The age distribution of IDU (IV drug users) cadavers indicated that the percentage of IDU (IV drug users) cadavers in the reproductive (20–40 years old) age was 80%. *Conclusion:* The greater prevalence of the HIV and HBV infection especially in the reproductive age of IDUs (IV drug users) indicates that the authorities need to pay more attention to prevention and harm reduction programs. *References:* 1. Rahimi Movaghar A, Mohammad K, Razzaghi EM. Trend of drug abuse situation in Iran: a three decade analysis. Hakim Research Journal 2002; 5:171–82.

110. Evaluation of the Influence of Glutaraldehyde on the Respiratory System on the Basis of Changes in Clara Protein Concentrations in Blood Serum of Medical Staff Employed in Endoscopic Theatres

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Objective: Evaluation of the influence of glutaraldehyde on the respiratory system on the basis of spirometry and changes in Clara protein concentrations in serum of persons occupationally exposed. *Methods:* Study included 40 persons employed in endoscopic theatres, exposed to glutaraldehyde. Twenty healthy persons, unexposed to glutaraldehyde or other factors with potential pulmonary toxicity constituted the control group. Forty persons from the studied group underwent medical examination, spirometry at rest at the beginning of first day of the working week (Monday, 8:00) and at the end of the last day (Friday, 14:00) with the spirometer Vicatest P2A, Mijnhardt, Holland and evaluation of Clara protein concentration in the serum, measured at the beginning and at the end of workweek with exposition to glutaraldehyde (latex - immunological method). The same tests were performed in the control group in the absence of exposition to harmful factors for the respiratory system. *Results:* Glutaraldehyde concentration in the air of endoscopic theatres did not exceed the threshold limit value during the period of study (0.32 ± 0.08 mg/m^3). Five per cent of persons employed there complained of symptoms suggestive of the presence of occupational allergy in the form of bronchial asthma, with associated allergic rhinitis. Lower concentrations of CC16 protein in serum (11.4 ± 4.7 micrograms/L) of patients exposed to glutaraldehyde were observed in comparison to those in serum of unexposed ones (13.8 ± 5.4 micrograms/L). Lower concentrations of CC 16 protein were measured in serum samples obtained from nurses on Friday (11.5 ± 4.3 micrograms/L) than those measured in subgroup of physicians (11.9 ± 4.3 micrograms/L). *Conclusion:* Presented results may indicate the usefulness of Clara protein level measurement as a biomarker of toxic effects of exposure of the respiratory system to glutaraldehyde.[1] *References:* 1. Palczynski C, Walusiak J, Krakowiak A, et al. Glutaraldehyde-induced occupational asthma: BALF components and BALF and serum Clara cell protein changes due to specific inhalatory provocation test. Occup Med 2005; 55:572–4.

111. Randomised Comparison Study of Intramuscular Droperidol Versus Midazolam for Violence and Acute Behavioural Disturbance in the Emergency Department - the DORM Study

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Objective: To determine the most effective and safest drug for intramuscular sedation in violent and acute behavioural disturbance (VABD) in the emergency department. *Methods:* We conducted a blinded randomised, comparison trial of intramuscular sedation for VABD, comparing droperidol (10 mg), midazolam (10 mg) and droperidol (5 mg)/midazolam (5 mg). Inclusion criteria were patients requiring physical restraint and parenteral sedation. The primary outcomes were duration of the VABD and time until further sedation using a survival analysis. Secondary outcomes were a reduction in the altered mental status score at 20 minutes, number of and type of injuries to the patient or staff members, further calls to security staff for assistance and any drug-related adverse effect. Electrocardiograms were obtained in all patients and the QT measured. *Results:* Of 91 patients included, 33 received droperidol, 29 received midazolam and 29 received the droperidol/midazolam combination. The median duration of the VABD was 20 minutes (interquartile range [IQR]:11–37min) for droperidol, 24 minutes (IQR:13–35min) for midazolam and 25 minutes (IQR:15–38min) for the combination (p = 0.91). Additional sedation was required in 11 (33%) droperidol patients, 18 (62%) midazolam patients and 12 (41%) in the combination group (p = 0.068). The hazard ratio for additional sedation in the midazolam versus droperidol group was 2.25 (p = 0.03), and for the combination versus droperidol was 1.29 (not significant). Patient and

staff injuries and further requirement for security did not differ between groups. The number sedated at 20 minutes was 24 (73%) in the droperidol group, 15 (52%) in the midazolam group and 23 (79%) in the droperidol/midazolam group (p = 0.061). There were two adverse effects for droperidol (6%), eight for midazolam (28%) and two for the combination (7%) (p = 0.02). An abnormal QT occurred in 2/31 (6%) droperidol patients which was not different from the other groups (p = 0.54). No arrhythmias occurred. *Conclusion:* Intramuscular droperidol was more effective than intramuscular midazolam for sedation in patients with VABD. Midazolam caused significantly more adverse effects due to over-sedation and droperidol was safe with no evidence of QT prolongation related to its use.

112. Risk Factors for Paracetamol (Acetaminophen) Hepatotoxicity

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Introduction: Paracetamol (acetaminophen) is the most frequent drug taken in overdose in the United Kingdom. Hepatotoxicity from paracetamol poisoning remains an important public health issue worldwide. Acetylcysteine is an effective antidote, especially if administered within a few hours of overdose, with need for treatment determined from the plasma paracetamol concentration and time since ingestion. This method identifies most patients at risk, but a few patients below usual treatment thresholds develop unexplained hepatotoxicity. The reasons for this apparently enhanced individual susceptibility are not fully understood, but there is accumulating evidence that certain clinical factors affect risk of hepatotoxicity after overdose. *Methods:* Literature review, concentrating on epidemiological studies of human paracetamol poisoning. Hepatic enzyme induction: Metabolic activation of paracetamol in man may occur via several hepatic isoforms including CYP2E1 and CYP1A2. These enzymes may be induced by drugs or chronic ethanol intake. Enzyme inducing drugs increase susceptibility to paracetamol hepatotoxicity in animals, while enzyme inhibitors may be protective.[1] There are many reports of unexpected hepatotoxicity in recipients of enzyme-inducing drugs, but epidemiological evidence of increased risk in man is lacking. For ethanol, there is evidence from several epidemiological studies that chronic excessive use increases risk of clinical complications including hepatitis, encephalopathy, hepatic coma and death,[2–6] and biochemical abnormalities such as raised plasma creatinine concentrations or acidosis.[2] However, not all studies have demonstrated enhanced toxicity in chronic ethanol users.[7,8] Interpretation is hampered by the fact that many of these studies are retrospective in design, important information may not be available and it may be difficult to eliminate potential sources of bias, such as alcoholics presenting late, inaccuracy in obtaining a history or presence of starvation (see below). Some recent studies have demonstrated increased incidence of liver function abnormalities in overdose patients who have not ingested any ethanol at the time of their overdose,[4,9] although available evidence is conflicting.[5] Starvation. Animal studies demonstrate reduced paracetamol glucuronidation and enhanced toxicity with starvation. In one study of human paracetamol poisoning, 8 out of 10 patients taking moderate overdoses of paracetamol (4–10 g) who developed liver failure had been fasting; this was more common than recent ethanol use in this group.[10] Age. In a Danish study, patients over 40 years old had an increased risk of fulminant hepatic failure and death, which was not fully accounted for by later presentation, later antidotal treatment or increased prevalence of ethanol use. Paracetamol metabolism does not appear to be affected substantially by age; enhanced toxicity could result from reduced functional liver reserve.[11] Tobacco use. In a further analysis of data from the same unit, an increased risk of hepatic encephalopathy and death was independently associated with current tobacco use.[12] It remains uncertain if this is related to induction of liver enzymes, e.g. CYP1A2. Underlying liver disease. In a study involving over 1,500 patients with paracetamol overdose, underlying liver disease was one of several factors associated with hepatotoxicity.[6] However, there was also increased risk associated with acetylcysteine treatment, suggest some residual confounding. Race. In a study involving 322 American children, risk of hepatocellular injury following paracetamol ingestion was increased in children of white race, as well as in older children, those presenting late and those with intentional overdose. Again, some confounding influences may not have been adequately addressed in the analysis.[13] *Conclusion:* The complexities of paracetamol toxicology and observed species differences make prediction of risk factors for human poisoning difficult. Epidemiological studies in human poisoning do suggest some factors that appear to confer increased risk, although the possibility of persisting confounding or bias cannot be excluded with certainty. More detailed prospective studies would be useful, but in the meantime lower treatment thresholds should be considered for patients with chronic excess ethanol ingestion and those who present without ethanol alcohol ingestion or having been fasting, who take enzyme inducing medication, who have evidence of underlying liver disease, or who are older. *References:* 1. Prescott LF. Paracetamol, alcohol and the liver. Br J Clin Pharmacol 1999; 49:291–301. 2. Bray GP, Mowat C, Muir DF, et al. The effect of chronic alcohol intake on prognosis and outcome in paracetamol overdose. Hum Exp Toxicol 1991; 10:435–8. 3. Wang K, Huang YS, Deng JF, et al. Characteristics and risk factors of acetaminophen-induced hepatitis in Taiwan. Zhonghua Yi Xue Za Zhi (Taipei) 1999; 62:369–75. 4. Schmidt LE Dalhoff K, Poulsen HE. Acute versus chronic alcohol consumption in acetaminophen-induced hepatotoxicity. Hepatology 2003; 35:876–82. 5. Schiødt FV, Lee WM, Bondesen S, et al. 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113. No Evidence of Hy's Law in Patients Treated with Labeled Doses of Acetaminophen in Prospective Clinical Trials

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Objective: In July 2009, US Food and Drug Administration (FDA) issued guidance for industry for the premarketing clinical evaluation of drug-induced liver injury, including Hy's Law criteria: hepatocellular injury [alanine or aspartate aminotransferase (ALT or AST, respectively) elevations >3X upper level of normal (ULN)], concomitant elevation of serum total bilirubin >2X ULN, and lack of other causality for elevated aminotransferases or total bilirubin. We retrospectively analyzed data from McNeil-sponsored, long-term clinical studies with acetaminophen for cases meeting FDA's definition of Hy's Law. *Methods:* McNeil-sponsored prospective, double-blind, randomized, placebo or active controlled clinical studies were reviewed. Studies ≥4 weeks duration, administering ≥3000 mg/d acetaminophen monotherapy, were included. Data from patients with baseline liver enzyme values >ULN were excluded. To account for variability among assay methods, reference ranges, and definition of ULN, the ULN used by each laboratory was considered when determining 3X ULN. Data were retrospectively analyzed to identify any cases meeting FDA's definition of Hy's Law. *Results:* Of 2512 subjects enrolled in 10 studies, 1928 met inclusion requirements and were analyzed per Hy's Law criteria. Patients, ages 20 to 85 years, received 3000–4000 mg/d acetaminophen, 1200–1600 mg/d ibuprofen, 660–750 mg/d naproxen, 972–2600 mg/d aspirin, or placebo. ALT or AST >3X ULN was observed in 10/953 acetaminophen, 1/168 aspirin, 1/444 placebo, 0/376 naproxen, and 0/216 ibuprofen patients. No patient in any treatment group met Hy's Law criteria for hepatotoxicity. While ALT or AST elevations >3X ULN were observed, these were transient and not accompanied by increases in total bilirubin >2X ULN or associated with hepatic failure. *Conclusion:* In prospectively designed, well-controlled studies in patients receiving 3000 mg to 4000 mg acetaminophen daily, no patients met Hy's Law criteria for drug-induced liver injury. Although some patients treated with acetaminophen had low-level ALT elevations, these elevations usually resolved or decreased with continued treatment, were unaccompanied by signs or symptoms of liver injury, and as such appear to be clinically insignificant. When used at maximum labeled doses of 4000 mg daily, evidence supports that acetaminophen does not cause hepatic failure or hepatic dysfunction.

114. Cyclophilin A is a Key mediator of Paracetamol Poisoning

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Objective: Paracetamol poisoning is a common clinical problem. Previously, we identified cyclophilin A (CypA) as a mediator of sepsis.[1] This effect was mediated via the extra-cellular CypA receptor CD147. As CypA is an abundant intra-cellular protein it is likely to be released from cells injured by paracetamol. Our hypothesis was that CypA mediates paracetamol poisoning via neutrophil recruitment into the injured liver. The specific aims were to determine whether: 1) CypA is pro-inflammatory; 2) CypA mediates paracetamol-induced liver injury; 3) an anti-CD147 antibody inhibits the neutrophil influx induced by necrotic liver cells and 4) CypA is released during paracetamol-induced liver injury in humans. *Methods:* To test aim 1 we incubated CypA with human blood and measured interleukin-6 release. For aims 2 and 3, C57BL/6 mice were injected with an anti-CD147 (or an isotype control) antibody (25 μg) 2 hours prior to injection with lipopolysaccharide (100 μg), necrotic liver (36 mg) or paracetamol (350 mg/kg). Six hours later the peritoneum was lavaged and myeloperoxidase was measured. For the paracetamol-injected mice, blood alanine transaminase levels were measured. To test aim 4 we collected samples from patients presenting with a paracetamol overdose. The concentration of CypA was determined by immunoblotting. *Results:* We found that CypA was pro-inflammatory (recruiting neutrophils in response to necrotic liver cells) and mediated paracetamol-induced liver injury in mice. Consistent with its release from necrotic cells, CypA was elevated in patients with paracetamol-induced liver injury. All results were statistically significant. *Conclusion:* In paracetamol poisoning, CypA is a novel drug target and potential biomarker. We are now breeding transgenic mice lacking CypA to further characterize the role of CypA in paracetamol poisoning. *Reference:* 1. Dear

JW, Leelahavanichkul A, Aponte A, et al. Liver proteomics for therapeutic drug discovery: Inhibition of the cyclophilin receptor CD147 attenuates sepsis-induced acute renal failure. Crit Care Med 2007; 35:2319–29.

115. Investigation of Neurological Toxicity of Poisoning with Alcohols

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Objective: Toxic alcohol poisoning may be complicated by serious neurological complications. They are mainly due to the formation of toxic metabolites. The objective of this review is to illustrate the different techniques of neurological investigation of these severe neurological disturbances. *Results:* Methanol poisoning results in severe metabolic acidosis due to formic acid accumulation that usually becomes critical after a delay of several hours. The main neurological findings are an impaired consciousness evolving to a deep coma, and to major visual disturbances ranging from blurred vision to blindness. Methanol-related brain injury involves basal ganglia, mainly the putamina. These lesions can be demonstrated either by brain computed tomography (CT) or magnetic resonance imaging (MRI). The different sequences of MRI appear particularly appropriate to investigate the topography and nature of methanol-related injury. The T1-weighted images are enhancing the fatty component of the tissues, while the T2-weighted images are enhancing the water component. The diffusion-weighted imaging is a specific technique for tissue contrast generation in which the original signal intensity is diminished proportionally to the degree of free-water diffusivity. The initial CT imaging studies demonstrated that putaminal necrosis with haemorrhage was present in a significant number of cases. MR studies have shown that in addition to putaminal lesions exhibiting abnormal hypersignal intensity of the lateral margins of the nuclei, parenchymal changes can extend to other areas (lentiform nuclei, corona radiata, centrum semi-ovale, hippocampus, cerebellum).[1] There is also an involvement of the subcortical white matter within frontal and/or occipital lobes. The diffusion-weighted sequence will reveal areas of decreased apparent diffusion coefficient (ADC) values in both putamina and in the white matter. This would reflect cytotoxic cell swelling. Such abnormalities are not, however, specific for methanol poisoning. As suggested by nonhuman primate studies, ocular toxicity is usually biphasic. Early retinal dysfunction can be diagnosed by electroretinography (ERG). Retinal dysfunction is potentially reversible and a relationship can be found between ERG changes and blood formate concentrations, with a threshold value for retinal dysfunction. It may be followed after a delay of several hours or days by a toxic optic neuropathy. Visual injury is well investigated by visual evoked potentials.[2] The risk for developing permanent visual injury is well correlated with the severity of metabolic acidosis and with the peak value of blood formate concentration. Ethylene glycol (EG) may induce by itself a significant central nervous system (CNS) depression; however, neurotoxicity is mainly related to the biotransformation of EG into several toxic metabolites responsible for severe metabolic acidosis. In addition to coma due to brain edema, EG poisoning may be complicated by cranial nerve palsies and severe axonal polyneuropathy. A limited number of patients has been investigated either by brain CT or MRI. On CT images, hypodense areas are seen in the central white matter, the basal ganglia, thalami, midbrain and upper pons. As in methanol poisoning, putaminal cystic necrosis can be observed on MR images. Nonspecific white matter abnormalities were also described. Diethylene glycol (DEG) has caused epidemic poisoning when it was substituted in pharmaceutical preparations. It appears likely that the principal metabolite of DEG, 2-hydroxyethoxyacetic acid (HEAA) is the major contributor to renal and neurological toxicities. In patients who eventually recovered from metabolic acidosis and acute renal failure, neurological complications can be delayed until at least 5–10 days post-ingestion. The most common neurological features are: progressive lethargy, bilateral facial paralysis, dysphonia, dilated and non-reactive pupils, loss of the gag reflex, and loss of visual and auditory functions.[3] In addition to sensorimotor injuries, there is also evidence of CNS involvement. In at least one patient, MRI identified abnormal foci in parietal and occipital lobes and in cerebellar hemispheres, possibly as a result of either edema or infarction. Peripheral neuropathies are effectively investigated by electromyography (EMG) and nerve conduction velocity (NCV) studies. Not all EMG/NCV studies have shown evidence of nerve demyelination. An acute axonal neuropathy may precede the development of a delayed demyelinating neuropathy. The analysis of the cerebrospinal fluid (CSF) is probably not helpful, as CSF proteins concentration may be normal even in the presence of demyelination. *Conclusion:* Toxic alcohol poisoning may be complicated by either central or peripheral neurological complications. The brain injuries should be preferentially investigated by MRI. However, the radiological findings are not totally specific for any alcohol poisoning, and the relationship with the clinical outcome is usually weak. *References:* 1. Hantson P, Duprez T. The value of morphological neuroimaging after acute exposure to toxic substances. Toxicol Rev 2006; 25:87–98. 2. Hantson P, de Tourtchaninoff M, Simoëns G, et al. Evoked potentials investigation of visual dysfunction after methanol poisoning. Crit Care Med 1999; 27:2707–15. 3. Schep LJ, Slaughter RJ, Temple WA, et al. Diethylene glycol poisoning. Clin Toxicol 2009; 47:525–35.

116. Acute Cholestatic Liver Injury Caused by Alcohol Contaminated with Polyhexamethyleneguanidine

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Objective: Acute poisoning with the antiseptic liquid, Extrasept-1, and some other liquids with the same structure was widespread in 44 regions of Russia in the period of August 2006 - May 2007 with more than 12.5 thousand patients; the mortality rate was 9.4%. This liquid contained ethanol, diethyl phthalate and polyhexamethyleneguanidine hydrochloride (PHMG-hydrochloride) in the amount of 0.1–0.14% which was confirmed by different methods including HPLC and GLC. PHMG-hydrochloride is a cation-active polymeric compound with a molecular weight ranging from 1,000 to 3,000 Daltons. *Methods:* Retrospective analysis of the symptoms and outcome was performed in 4 Poison Centres in the cities: Perm, Ekaterinburg, Irkutsk and Khabarovsk. *Results:* We observed 579 patients (215 females and 364 males) with similar symptoms in 4 centres. Mild symptoms developed in 2.5% of cases, moderate in 63%, severe in 24% and fatal in 10.5%. The main symptoms on admission included jaundice (99.7%), skin itch (78.4%), weakness (96%), anorexia (65.8%), dizziness (65.6%), nausea (54.8%), vomiting (22.6%), stomach-ache (52.7%), diarrhea (32%) and fever (50.1%). Laboratory data showed on average (mean ± standard deviation): total bilirubin 15.0±9.6 mg/dL, direct bilirubin 10.7 ± 6.6 mg/dL cholesterol 13.3±8.3 mmol/L, alanine aminotransferase 179.9±135.4 U/L, aspartate aminotransferase 138.5±188.9 U/L, alkaline phosphatase 1150.1 ± 776.3 U/L, gamma-glutamil-transpeptidase 1707.0 ± 1505.7 U/L. Leucocytosis more than 10,000 /mcL was present in 22.7% of patients and the hemoglobin level was less than 100 g/L in 20.6% of cases. During observation 2.3% of patients developed psychosis, 4.7% became confused and 1.6% comatose. Bleeding was observed in 3.6% of cases. The patients recovered during a period of from 1 to 5 months but the high level of alkaline phosphatase and gamma-glutamil-transpeptidase were estimated after 6 - 12 months in patients whom we managed to examine after discharge. Sixty-one patients died of brain edema or heart failure 1 to 5 months after poisoning. Local cholestasis, inflammatory infiltration and fibrosis developing into cirrhosis were found out by liver biopsy or postmortem liver microscopy. *Conclusion:* Acute liver injury caused by PHMG-hydrochloride can be characterized as cholestatic hepatitis with a severe inflammatory component and it caused a high rate of mortality.

117. Osmolar Gap Method for Predicting Toxic Alcohol Levels in Pooled Serum

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Objective: To evaluate the accuracy of the Osmolar Gap (OG) method for predicting concentrations of four toxic alcohols (TA): methanol (ME), ethylene glycol (EG), isopropanol (ISO), and diethylene glycol (DEG). *Methods:* Frozen pooled serum samples were thawed and then spiked with known quantities of DEG, ISO, ME, and EG, attempting to replicate concentrations encountered in accidental poisoning situations. Serum was divided into 4 groups, one for each TA, with 4 tubes in each group. In each group, tubes were spiked with the TA to target a final [TA] of 25 mg/dL; 50 mg/dL; 100 mg/dL; and 200 mg/dL. Serum osmolality, Na, BUN, glucose were measured; serum osmolarity was calculated using the formula: 2Na + BUN/2.8 + glucose/18 for all specimens. The calculated osmolarity was subtracted from the measured osmolality to calculate the OG, and OG was multiplied by 1/10 the MW to estimate the concentration of the TA. The TA concentrations were measured by GC/FID. *Results:* For all TA tested, low levels (<50 mg/dL) did not raise the OG above the normal range. When OGs were ≥ 20 mOsm/L, the predicted TA level had a similar percentage error among all alcohols (range 3–36%). For a measured DEG level of 167, the OG method predicted a level of 204 (22% error); a measured EG level of 175, OG method predicted 239 (36%); measured ISO levels of 163 and 83, OG predicted 167 and 105, respectively (2 and 28% error); and measured ME levels of 167 and 86, OG predicted 162 and 89 respectively (both 3% error). *Conclusion:* This provides experimental support that low, but clinically significant TA levels, in the range of 25–100 mg/dL, cause OG values within the expected normal range (± 10 mOsm/L) and cannot reliably predict TA levels. When OG is very elevated (>20), the OG method can be useful, and has a percentage error of 3–36%. For the larger molecular weight alcohols (DEG, EG) only serum levels >150 mg/dL elevated the OG above the normal range. The OG method is as accurate for DEG as it is for the other toxic alcohols.

118. Formate Analyses: A Research Tool of Limited Interest, or a Diagnostic Tool in the Clinical Setting?

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Introduction: Methanol remains one of the most toxic substances according to morbidity and mortality. Specific and efficient treatments exist, but poor outcome is related to the often delayed diagnosis and treatment. Diagnosis is often difficult in these patients who frequently present comatose with a metabolic acidosis of unknown origin. The clinical features are often mistaken for other medical diagnoses, and the lack of antidotal treatment may often lead to death. The poisonings often presents as outbreaks (especially in the developing world), or as single suicide attempts. Specific analysis (S-methanol) is available only in specialized centres, it is time consuming and seldom available on a 24 hours basis. Further, the mostly commonly used substitute (the osmolal gap) is hardly ever available outside the western world. Added to that is the fact that many methanol poisoning incidents occur in developing countries where resources for diagnostics and therapeutics for

these poisonings are limited. The diagnosis of methanol should hence be based upon more easily available methods that are cheaper and adaptable to analytical equipment already present: S-formate can easily be measured on most of the commonly available spectrophotometers using reagents commercially available. The method is fairly cheap, well tested and has a high specificity and sensitivity. The method itself is simple and was established many years ago,[1] being based on an enzymatic reaction with the highly specific enzyme formate dehydrogenase (FDH), By catalyzing the reaction where formate is oxidised to CO_2 and water, and NAD^+ is reduced to NADH, a typical spectrophotometric method frequently found in most hospitals can measure the amount of NADH produced at the standard wavelength of 340 nM. The method is highly specific and sensitive, but it has only been used for scientific purposes until recently. *Results:* A prospective study in Norway recently used it in 15 methanol poisoned patients in order to evaluate the method, as well as the S-formate level compared to the clinical findings. All 15 had increased S-methanol, 10/15 had symptoms, 14/15 had increased S-formate, indicating that S-formate was detectable in 4/5 patients before symptoms started. This is supported by the fact that the endogenous level of formate in the body is <0.4 mM (<2 mg/dL), whereas the symptoms usually do not appear before S-formate is 8–12 mM (40–60 mg/dL) or more, which represents a 20-folds increase or more.[2] *Discussion:* The formate tool is a well known analytical method in basic sciences, whereas the use in clinical practice is limited to the research objectives. However, the method is easy to perform, only needs readily available ingredients, and can be used on analytical apparatus available most places. It is cheap and has a high sensitivity and specificity. Further, it is well known that the toxic effect of methanol is due to formate, hence no formate produced - no toxicity. The clinical symptoms appear at a 20-fold level of the upper endogenous level. The only prospective study performed until now in patients showed the clinical benefits of having such a tool available and at hand. By adapting this simple method in clinical practice, a diagnosis can be established within less than half an hour. The main obstacle seems to be the awareness of this simple method in the clinical setting. We have suggested making a kit containing all the necessary ingredients (containing the formate dehydrogenase enzyme, NAD^+, a calibrator, two controls and a how-to-do list). This will simplify the spread of the method further. *Conclusion:* S-formate analysis is a highly specific and sensitive method that can be used on most commonly available spectrophotometers. It is cheap, fast and simple, and the greatest obstacle seems to be the lack of knowledge of the method in various centers. It can greatly simplify the diagnostics in the clinical setting, and is also applicable to developing countries. *References:* 1. Schaller KH, Triebig GT. Formate Determination with Formate Dehydrogenase. In: Bergmeyer HU, ed. Methods of enzymatic analysis. Weinheim, Germany: Verlag Chemie, 1984:668–72. 2. Hovda KE, Urdal P, Jacobsen D. Increased serum formate in the diagnosis of methanol poisoning. J Anal Toxicol 2005; 29:586–8.

119. A Critical Review of Using the NPDS Data Collection for Research Purposes

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Objective: Poison control centers worldwide collect vast amounts of surveillance data. These have a variety of important potential research uses in addressing public health and health policy issues in clinical toxicology. In the United States, the National Poisoning Data System (NPDS), maintained by the American Association of Poison Control Centers (AAPCC), uploads real-time, template-generated case data from all U.S. poison control centers. The purposes of this review are to: 1. identify characteristics of an ideal toxicology surveillance system, 2. describe the current NPDS system 3. give examples of the research uses of the NPDS database 4. explore the advantages, shortcomings, and potential pitfalls in conducting such epidemiological research using NPDS data. *Discussion:* The example of carbon monoxide illustrates well the generic pyramid flow of appropriate databases for the secondary analysis of toxicology-related issues. At each population stratum of interest, the data can be parsed starting with attitudes and behaviors regarding prevention, total population exposures, out-patient department visits, emergency department cases, hospitalized patients, and deaths. Concepts of ideal surveillance instruments used for such purposes include ease of capture ("routine" ness), timeliness, low cost, active, representative population-based reporting, weighted sampling, consistency, accuracy, flexibility, comprehensiveness, capacity for linkage, and geospatial capability. Synopsis characterizes how broad in scope a 'landscape' view of the population can be attained at a single point in time by integrating diverse data elements. For NPDS, current data elements include time, date, call type, location, age, gender, exposure duration, cause, route, symptoms, severity, and treatment. The 'hazard factor' is a derived parameter allowing comparison of relative severity between products in the database. NPDS data have been used to: 1. identify new populations at high risk for poisoning; 2. conduct post-marketing surveillance of adverse drug reactions; 3. review frequency of different poisoning management strategies, including antidotes; 4. identify emerging public health epidemics (clusters and anomalies); 5. inform clinical practice guidance and public health policies. Such data have been used to define vulnerable populations, identify emerging epidemics, conduct post-marketing surveillance of drugs and commercial products, inform changing patterns of poisoning exposures over time, and define poisoning prevention needs. Methods research and hypothesis-generating studies are also possible using NPDS. Comparative research, using NPDS and other databases, such as Medwatch data from the FDA, can add perspective and context, depending on the question being posed. NPDS requires ongoing maintenance to preserve its integrity; evaluation for its shortcomings, such as technical difficulties, coding variability, reporting variability between poison centers, inter-rater reliability, duplicate files, missing data, etc. must be addressed in planning new research initiatives. The AAPCC disclaimer required for all such publications describes the fundamental caveat associated with utilizing NPDS data for research. NPDS is appropriate for some research designs, such as case series, cross-sectional studies, cluster analyses, and those looking either prospectively or retrospectively at trends in the frequency of occurrence over time. NPDS would not be an appropriate tool to address research hypotheses requiring prospective controlled trials, although it could be the source of preliminary data in preparation for such studies. *Conclusion:* NPDS has great potential for use in well-designed research studies to address appropriately-tailored research questions or hypotheses. *References:* 1. German RR, Armstrong G, Birkhead GS, et al. Updated guidelines for evaluating public health surveillance system: recommendations from the guidelines working group. MMWR 2001; 50:1–35. 2. Chu AF, Marcus SM, Ruck B. Poison control centers' role in glow product-related outbreak detection: implications for comprehensive surveillance system. Prehosp Disaster Med 2009; 14:68–72. 3. Derby MP, McNally J, Ranger-Moore J, et al. Poison control center-based syndromic surveillance for foodborne disease. MMWR 2005; 54:35–40. 4. Spiller HA, Griffith JRK. The value and evolving role of the U.S. Poison Control Center System. 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120. Observational Studies are Hampered by 'Lost to Follow-up'. How to Perform Better?

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Objective: Observational research is important in clinical toxicology, because there are many ethical and practical reasons why randomized clinical trials are difficult to perform. Our Poisons Information Centre (NPIC) uses observational methods to study dose response relationships, and, for instance, the impact of legislation. The number of patients lost to follow-up (LFU) is a major problem of these kind of studies. Therefore we performed an evaluation on the causes of LFU, with the ultimate goal to reduce the number of LFU. *Methods:* Six prospective case consecutive NPIC studies with different study designs for data collection were analyzed for LFU and compared. LFU is defined as patients that are eligible for the study but for whatever reason are not included, or patients lost to follow-up despite initial inclusion. *Results:* Table 1 presents the percentages of LFU together with the main

Table 1. Percentages of patients lost to follow-up together with main reasons

Study	Data collection design	LFU	Main reasons for LFU
XTC	Physician and patient interviewed at a bed-site visit performed by dedicated researchers.	18%	- physician refused to participate: 37% - patient refused to participate: 18% - patient left hospital before interview: 37%
Occupational poisoning	Patient interviewed at work by dedicated researchers.	20%	- LFU was totally due to refusal of patients or companies to participate
Lamp oil	Physician and patient or caregiver interviewed via a telephone call performed by dedicated researchers.	28%	- physician refused to participate: 14% - patient or caregiver refused to participate: 0% - interview impossible because of inadequate information to contact physician or track patient: 81%
Xylometazoline	Physician interviewed via a telephone call performed by information specialists.	41%	- physician refused to participate: 10–20% - interview impossible because of inadequate information to contact physician or track patient: 70–80%
ADHD medication	Physician interviewed via a telephone call performed by information specialists.	44%	- physician refused to participate: 10% - interview impossible because of inadequate information to contact physician or track patient: 90%
(Es)citalopram	Physician interviewed via a telephone call performed by information specialist.	48%	- physician refused to participate: 12% - interview not possible because of inadequate information to contact physician or track patient: 81%

reasons. *Conclusion:* This evaluation illustrates that in observational studies the data collection method used influences the number of patients lost to follow-up. In order to reduce the number of LFU and thereby increase the quality of the study, the following considerations can be taken into account. If physicians and patients are visited by dedicated researchers this results in the lowest percentages of LFU. However this is an expensive and time intensive method. Using phone interviews performed by dedicated researchers is a suitable alternative. Most important is to obtain sufficient information at the first contact, in order to be able to contact the physician or patient for further information.

121. Poisoning Risk Caused by Cleaning Products and Detergents

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Objective: Cleaning product or detergent exposures are frequent causes of poisons centres' (PC) advice. Although product safety has increased tremendously during the last decades there is still concern about poisoning hazards, especially in some product groups. This study is directed to quantify the poisoning risk for Germany. *Methods:* All exposures to cleaning products or detergents reported to the authors' poisons centre between 1999 and 2008 were selected from the PC case database. Cases were analysed for groups of agents involved and poisoning severity. An 'IntoxIndex' was calculated for all agent groups, by dividing the sum of all moderate, severe or lethal poisonings, by the number of all exposures. *Results:* Within the study decade 26,268 exposures to cleaning product or detergent were identified corresponding to 10.0% of all exposures recorded. In 66% no symptoms, in 22% minor symptoms were reported, 2% of all cases were considered as moderate or severe. There were 9 lethal cases, of which 3 cases were of unclear causal relationship to the exposure. In 10% of all cases severity could not be evaluated. The overall IntoxIndex was calculated as 2.1%. Table 1 breaks down the cases with relation to agents involved indicating that most cases were reported for manual dish washing products, while drain cleaners (IntoxIndex = 17.4%), industrial cleaners (IntoxIndex = 12.9%) and milking machine cleaners (IntoxIndex = 16.7%) were the product groups with the highest poisoning risks. *Conclusion:* Cleaners and detergents are comparatively safe products, but for some agents the risk of causing substantial poisoning is still high.

Table 1. Agents involved and severity

severity vs. product group	lethal	severe	mode-rate	minor	no	unknown	sum of expos.	Intox Index
lavatory cleaners	3	13	88	860	2132	401	3485	2.9 %
drain cleaners	1	21	71	223	81	137	534	17.4 %
oven cleaners	1	7	23	158	254	76	519	6.0 %
manual dish washing products	1	6	20	868	3969	243	5107	0.5 %
all purpose cleaners	1	5	30	604	1639	212	2491	1.4 %
automatic dish washing products	1	2	17	379	1675	144	2218	0.9 %
descalers	1	–	10	666	2781	156	3614	0.3 %
industrial cleaners	–	8	32	118	49	103	310	12.9 %
laundry detergents	–	4	9	320	1688	106	2127	0.6 %
glass cleaners	–	4	25	215	695	81	1020	2.8 %
metal cleaners	–	4	20	109	176	78	387	6.2 %
shoe and leather care products	–	3	7	59	153	22	244	4.1 %
front wall and stone cleaners	–	2	12	74	51	52	191	7.3 %
laundry additives	–	2	8	199	616	78	903	1.1 %
paint removers	–	2	2	18	34	9	65	6.2 %
rinse aids for dishwasher	–	1	7	206	594	57	865	0.9 %
furniture care products	–	1	5	73	132	39	250	2.4 %
milking machine cleaners	–	–	18	41	16	33	108	16.7 %
soot removers	–	–	2	2	7	7	18	11.1 %
cleaners not specified	–	12	42	238	278	160	730	7.4 %
other cleaners	–	–	12	256	697	117	1082	1.1 %
sum	9	97	457	5686	17708	2311	26268	2.1 %

122. Safety Data Sheets Under the New REACH Regulation - More Useful for Poisons Information Centres?

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Objective: The current Safety Data Sheet (SDS) does not provide a detailed product composition. The toxicological information in the current SDS is limited or entirely missing. In order to be able to adequately inform about symptoms and treatment of acute intoxications, Poisons Information Centres (PIC) need detailed product information. Will the new SDS be appropriate for PIC use? *Discussion:* SDS under REACH Regulation: Improvements in the SDS are expected from the REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) Regulation that incorporated new requirements in Annex II. For registration of substances, the REACH Regulation requires a technical dossier (containing basic toxicological information) and for some substances a Chemical Safety Report (CSR) with a 'human health hazard assessment' (toxicokinetics, acute effects, irritation/corrosivity, amongst others) and exposure scenarios. Better information for registration will become available in SDS section 11. The exposure scenarios will appear in an Annex. When the new SDS is aligned with the Globally Harmonised System (GHS) in 2010 for substances and in 2015 for mixtures, the toxicological information will be further extended. The draft version of the forthcoming new REACH Annex specifically states that SDS section 11 is meant for medical professionals and toxicologists. For every health hazard classification, toxicological information should be included. If available, human data should be used. A further improvement is that if a mixture or substance is not classified for a particular hazard, it should be stated that data are lacking or data are inconclusive or insufficient for classification. The improved toxicological information in the new SDS is useful for PICs but a detailed product composition remains necessary. An important shortcoming of the new SDS for PIC use is that only dangerous substances above specified thresholds have to be mentioned. Because of missing guidelines, wide concentration ranges can be used. The consequence is that adequate risk assessment after exposure is seriously hampered. *Conclusion:* Under the REACH Regulation the SDS will improve. Poisons Information Services may benefit from these improved SDS. Nevertheless, a detailed product composition remains necessary. This is missing in the new SDS. Additional notification of the information should become obligatory.

123. Ingestion of Button Cell Batteries - Experiences of the Poison Information Centre Berlin. Proposal for a Therapy Guideline

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Objective: Ingestion of button cell batteries is a common cause for contacting us. Nevertheless there is no consistent therapeutic guideline. Therefore it seems to be necessary and important to evaluate our data from 2000–2008 to discuss and develop new strategies in diagnosis and therapy of button cell ingestion. *Methods:* We collected 1425 cases of button cell ingestions in the years 2000–2008. Mainly affected were children below the age of seven (91%) and 53% (=764) were between 1 and 3 years old. We analysed our data in regard to diagnostics, therapy and clinical outcome. *Results:* Severe complications (chemical burns, perforation, fistula) are rare and occur only if the button cell battery lodges in the oesophagus. There is no absorptive toxicity. In the monitored period we only had two cases with severe symptoms. First, a 9-month old baby where the button cell lodged in the oesophagus was not detected because there was only an abdominal x-ray performed. Second, an 11-month old girl where a doctor unsuccessfully tried to remove the button cell by magnetic tube. After endoscopic removal from the oesophagus there were already severe burns found. Beside those two severe cases there are only a few cases with mild to moderate symptoms reported (stomach pain, vomiting, melaena). Unfortunately we do not get feedback very often, especially if there are no or only mild symptoms. This leads to the assumption that, as described in literature, the majority of all ingested button cells pass the GI-tract quickly and generally without complication.[1] *Conclusion:* The great majority of all cases of button cell ingestion is harmless. Because of the rare but possibly severe complications we use the following approach: 1. All children with assumed ingestion must receive abdominal and thoracic x-ray. 2. If the battery is lodged in the oesophagus it should immediately be removed endoscopically. 3. In all other cases, passing through the gastrointestinal tract should be awaited controlling the stool. Only if symptoms occur or the transit time exceeds 7–10 days further diagnostic is required. *References:* 1. Litovitz T, Schmitz BF. Ingestion of cylindrical and button batteries: an analysis of 2382 cases. Pediatrics 1992; 89:747–57.

124. Mandatory Carbon Monoxide Detectors Do not Appear to Reduce the Incidence of Death from Carbon Monoxide Poisoning

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Objective: Carbon monoxide (CO) poisoning is a leading cause of unintentional poisoning deaths. In our region, CO detectors became mandatory 11/1/2004. The purpose of this study was to determine if this legislation changed the incidence of deaths reported to the Medical Examiner (ME). *Methods:* The ME's toxicology database was searched for all cases with postmortem CO concentrations from 1/1/1996 - 12/31/2008. A CO related death was defined as a COHb > = 30% without any other obvious cause of death. Cases were divided into pre and post regulatory periods. The number of deaths pre and post legislation were compared using a Wilcoxon rank sum test. In an attempt to control for historical variation in exposure risk, the annual incidence

of fires for the study period was obtained from the fire department. *Results:* Although there was a steady decline in CO related deaths during the entire period, the difference pre- and post-legislation was not statistically significant. There were 47 deaths in the pre-regulatory period and 33 deaths in the post-regulatory period ($p = 0.46$). There was no significant difference in mean number of deaths per month in 69 pre-regulatory months compared to 69 post-regulatory months (t-test $p = 0.073$). Structural fires decreased from 285,778 pre-regulatory to 265,935 in the post-regulatory period ($p = 0.073$). *Conclusion:* CO related deaths declined during study period possibly because of the overall decrease in structural fires. Mandatory CO detectors did not appear to have affected this trend. Lack of effect on mortality may relate to poor enforcement, inadequate maintenance of devices, intentional suicides, or deaths occurring in unmonitored areas such as empty warehouses, and reporting bias. A previous evaluation of poison center calls suggested that there was a decrease in reported major effects from CO following the legislation. This study is subject to all the limitations of a retrospective review of passively collected data. Notably the data may not reflect the true incidence of CO exposure, as all deaths may not have been reported to the ME. Future work is needed to elucidate the reasons for this trend.

125. Anaphylactoid Reactions to Acetylcysteine After Paracetamol Overdose

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Introduction: Acetylcysteine is widely used to minimize the risk of hepatotoxicity after acute paracetamol overdose. This paper reviews the occurrence of acetylcysteine adverse effects, risk factors and the likely underlying mechanisms. *Discussion:* Adverse effects occur in a high proportion of treated patients, which are variably reported to affect 5–15% of patients in retrospective studies, and 40–56% in prospective studies. Anaphylactoid reactions are characterized by erythema, urticaria, flushing, bronchospasm, wheeze, and hypotension.[1] Around 15–30% of patients develop a diffuse erythematous or urticarial rash, which typically affects the upper trunk, neck and face. The clinical presentation is similar to true anaphylaxis but important differences exist; namely, prior exposure to acetylcysteine is not required, and treatment can normally be reintroduced without provoking a further reaction. Onset is typically at 20–60 min after commencing intravenous acetylcysteine, and features subside quickly after stopping the infusion. Localized wheal and flare responses to acetylcysteine are concentration-dependent, and the incidence of anaphylactoid reactions may be reduced when the initial loading dose of acetylcysteine 150 mg/kg is administered over 60 or 90 min instead of the standard 15 min regimen.[2] Patients with co-existent asthma are at greatest risk of anaphylactoid reactions and more severe reactions, suggesting an immunological basis.[3] Histamine appears to be an important mediator, and wheal responses to localized acetylcysteine injection can be abolished by prior treatment with a selective histamine-1 receptor antagonist.[4] In a series of 362 patients treated with acetylcysteine within 24 hours of acute paracetamol overdose adverse reactions occurred in 147 patients (40.6%), including anaphylactoid reactions in 54 (14.9%), gastrointestinal symptoms in 90 (24.9%), and localized skin reactions at the infusion site in 3 patients (0.8%). The median time to onset of anaphylactoid reactions was 75 min (IQR: 50–112 min). An inverse relationship was found between serum paracetamol concentrations and occurrence of anaphylactoid reactions; a similar pattern was found when equivalent 4 hour paracetamol concentrations were considered so as to minimize for the confounding effect of interval between ingestion and treatment.[5] Paracetamol is capable of inhibiting cyclo-oxygenase isoenzymes and, for example, concentrations between 500–3000 µmol/L (76–453 mg/L) inhibit prostaglandin E2 synthesis in a dose-dependent manner. The lower occurrence of anaphylactoid reactions in patients with high paracetamol concentrations suggests a cyclo-oxygenase dependent mechanism.[5] Paracetamol also possesses antioxidant properties at supratherapeutic concentrations of 100 to 1000 µmol/L (15–151 mg/L), and can directly inhibit the vasodilator responses to arachadonic acid *in vivo*. True anaphylaxis is associated with increased circulating concentrations of histamine and tryptase due to mast cell degranulation. In a prospective study of acetylcysteine administration after paracetamol overdose, predefined categories were: minimal if patients had no reaction or mild gastrointestinal symptoms only, moderate if patients had symptoms requiring temporary cessation of infusion, mild flushing, pruritus, mild chest pain, breathlessness, or peak expiratory flow rate (PEFR) 25--50% less than baseline, and severe if acetylcysteine was stopped due to severe flushing, respiratory distress, moderate to severe chest pain, >50% reduction in PEFR from baseline, or hypotension (systolic blood pressure <90 mmHg or diastolic blood pressure <50 mmHg). In a series of 169 patients, severity was minimal in 101 (59.8%), moderate in 51 (30.2%), and severe in 17 (10.1%). Serum paracetamol concentrations were lower in patients with severe adverse effects: median (IQR) 46 mg/L (0–101 mg/L), moderate 108 mg/L (54–178 mg/L), minimal 119 mg/L (77–174 mg/L), $p = 0.002$.[6] Plasma acetylcysteine concentrations in a subset of patients were similar between patients with minimal, moderate and severe reactions (see Table 1). Plasma histamine concentrations were significantly higher in patients with moderate and severe reactions than those in the minimal group, although tryptase was not increased in any group.[6] These findings confirm the importance of histamine as a mediator of anaphylactoid reactions, but suggest that this is not attributable to mast cell release. *Conclusion:* Prospective studies identify a high rate of occurrence of adverse effects of acetylcysteine. Those at greatest risk include patients that present late, those with comparatively low serum paracetamol concentrations, patients with asthma, and those with a family history of allergy. The mechanisms are not fully elucidated but histamine is a critical component of the response, and cyclo-oxygenase activation might contribute to changes in vascular reactivity. *References:* 1. Bailey B, McGuigan MA. Management of anaphylactoid reactions to intravenous N-acetylcysteine. Ann Emerg Med 1998; 31:710–5. 2. Butera R, Georgatos J, Arrigoni S, et al. Adverse reactions to intravenous acetylcysteine: effects of reducing the infusion rate of the loading dose. Clin Toxicol 2005; 43:437–8. 3. Newton PJ, Thomas SHL. Anaphylactoid reactions to intravenous acetylcysteine, frequency, risk factors and outcome. Clin Toxicol 2006; 44:432. 4. Bateman DN, Woodhouse KW, Rawlins MD. Adverse reactions to N-acetylcysteine. Lancet 1984; 2:228. 5. Waring WS, Stephen AF, Robinson OD, et al. Lower incidence of anaphylactoid reactions to N-acetylcysteine in patients with high acetaminophen concentrations after overdose. Clin Toxicol 2008; 46:496–500. 6. Pakravan N, Waring WS, Sharma S, et al. Risk factors and mechanisms of anaphylactoid reactions to acetylcysteine in acetaminophen overdose. Clin Toxicol 2008; 46:697–702.

Table 1. Plasma acetylcysteine concentration determined at baseline and at 0.5, 2, 4 and 20 hours after commencing intravenous administration in patients with no or minimal anaphylactoid reaction, moderate, or severe reactions. AUC_{20} is the area under the time-concentration curve up to 20 hours. Data presented as median (interquartile range)

	Minimal n = 10	Moderate n = 4	Severe n = 8	Total n = 22
Baseline	3 (2–4)	5 (5–5)	4 (4–5)	5 (3–5)
0.5 h	94 (78–104)	98 (63–124)	95 (81–114)	95 (75–115)
2 h	45 (37–61)	43 (36–51)	37 (33–46)	40 (34–48)
4 h	32 (14–37)	41 (31–41)	35 (28–35)	34 (24–37)
20 h	16 (15–19)	25 (16–25)	17 (16–21)	17 (15–24)
AUC_{20}	58.6 (48.7–68.3)	60.4 (49.4–70.7)	52.0 (43.4–60.0)	56.2 (45.6–67.3)

126. Developing a New Administration Regimen for N-Acetylcysteine in Paracetamol Overdose Using Pharmacokinetic Simulations

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Objective: N-acetylcysteine (NAC) is an effective antidote for paracetamol toxicity. However, the current dosing regimen results in a large loading dose which is rapidly administered and thought to be associated with adverse reactions. The aim of this study was to develop a dosing regimen where NAC is commenced immediately on presentation at a slower rate of infusion. *Methods:* Studies of the pharmacokinetics of paracetamol and NAC were identified from the literature and used to build deterministic models of the pharmacokinetics of paracetamol and NAC in Microsoft Excel and NONMEM VI. Paracetamol overdoses were simulated at different doses and compared to the paracetamol nomogram. The pharmacokinetics of NAC were simulated for a patient presenting 2 hours after overdose. A potential treatment regimen was then developed by matching the area under the curve for a constant infusion rate of NAC commenced on admission with the two scenarios using the current protocol - 1) commenced when paracetamol concentrations above the nomogram are available; 2) commenced 8 hours post overdose. *Results:* Comparing simulated paracetamol plasma concentrations time curves to the nomogram showed that the required dose for paracetamol to intersect the nomogram at 4 and 8 hours was 23.8 g and 29.2 g respectively. The immediate commencement of NAC on presentation at a constant infusion rate of 14 mg/kg/hr provided a similar AUC of NAC to the traditional approach with 3 different infusion rates. However, this newer regimen avoided early high peak concentrations and in the second scenario allowed for earlier completion of treatment. *Conclusion:* Administering NAC at a constant rate immediately upon presentation to hospital avoids high peak concentrations and rapid infusion rates, while maintaining similar potential efficacy. The timing of the measurement of paracetamol concentrations may affect whether these are toxic or not, based on the nomogram for similar doses.

127. The Use of N-Acetylcysteine (NAC) in Poisonings Other Than Paracetamol

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Objective: N-acetylcysteine (NAC) has a well established role as the drug of choice in the treatment of paracetamol poisoning. Due to its wide range of apparently beneficial effects NAC has also been suggested for a number of other applications. To elucidate the present use of NAC in poisonings other than paracetamol, a survey has been undertaken. *Methods:* A questionnaire was sent out to all members of the EAPCCT and Medline was searched for relevant literature published 1990–2009. *Results:* Completed questionnaires were returned from 26 European poisons centres, three North American centres, one Australian centre and the Israeli centre. According to the survey NAC is currently considered to be useful, or worth trying, in the

treatment of poisoning by sixteen different agents or groups of agents. Poisoning with amatoxin containing mushrooms tops the indication list, with 13 centres in ten European countries and one in the USA recommending NAC to be used. Chlorinated hydrocarbons is a good number two with 12 centres advising NAC administration, eleven of these being located in seven European countries and one in the USA. Next come nitriles and paraquat with seven (Europe and USA) and six (Southern Europe, Israel and Australia) centres respectively being of the opinion that NAC treatment is motivated. Some centres advise NAC in the treatment of poisonings by essential oils (pennyroyal oil, clove oil), irritant gases, methyl ethyl ketone peroxide (MEKP), dimethylformamide (DMF), phenol, hepatotoxic plants and aflatoxin. Substances occasionally mentioned are monochloroacetic acid (MCA), potassium permanganate, chromium, caustics and xylitol (in dogs). A few centres recommend NAC in all poisonings causing liver damage. The rationales for advising treatment with NAC were: 1. Replenishment of glutathione levels and supply with sulfhydryl groups; 2. The antioxidant properties of NAC in acting as a scavenger of free radicals; 3. Possible benefit and little harm. Concerning the scientific evidence of the use of NAC in the different poisonings listed, numerous experimental studies (cell cultures and animals) studies are quoted while human data are sparse and commonly restricted to case reports. The review of the literature (the Medline search and the references given by the centres participating in the survey) may be summarized as follows; I. Amatoxin: There are experimental data indicating the efficacy of NAC as well as studies with negative results. Patient series from Italy[1,2] point towards a favourable effect and a comprehensive review of 2108 cases reported in literature[3] supported NAC as well as silibinin as effective therapies. II. Chlorinated hydrocarbons: Animal studies have demonstrated that NAC protects membrane lipids and proteins due to its direct radical scavenging properties and the use of NAC in clinical practice is since long accepted. III. Nitriles: The metabolism of aliphatic and olefinic nitriles (eg acrylonitrile) is followed by a delayed formation of cyanide. Administration of sulfur donors increases the cyanide metabolism. Acrylonitrile has also a toxic effect on the central nervous system which can be avoided by binding to NAC.[4] IV. Paraquat: The mechanism of paraquat toxicity involves the generation of reactive oxygen species leading to oxidative injury of the alveolar epithelium and subsequent fibrosis. Different antioxidants, including NAC, have in animals and cell cultures proved effective in counteracting the damage.[5] V. Essential oils: The metabolism is similar to that of paracetamol. So, when the major metabolic pathways are saturated reactive metabolites, depleting hepatic glutathione will form and liver damage may follow.[6] VI. Irritating gases: In animal studies intratracheal NAC protected against phosgene-induced lung injury by maintaining protective levels of glutathione and reducing lipid peroxidation. In a case series of seven patents exposed to high concentration of phosphine and treated with inhalation of cortisone and iv NAC the outcome was favourable.[7] VII. MEKP: Methyl ethyl ketone peroxide is an unstable organic peroxide that releases free oxygen radicals. Ingestion induces ulceration of the proximal digestive tract and liver necrosis. Acidosis and neurological symptoms may also occur due to accumulation of organic acids. Several experimental studies support the efficacy of NAC but human data are, so far, restricted to one case report.[8] VIII. MCA: NAC has been suggested based on experimental data on binding of MCA to acetylcysteine and other sulphydryl containing substances. VIIII. Miscellaneous: This group includes other agents depleting glutathione by forming reactive metabolites (DMF, aflatoxin, hepatotoxic plants, phenol - in small animals) and agents supposed to form reactive oxygen radicals (chromium, potassium permanganate, xylitol - in dogs). Generally the documentation of the benefit from treatment with NAC is even more insufficient or lacking in this group. Finally, four centres have ongoing or plan clinical studies on the efficacy of NAC. *Conclusion:* NAC is used in a wide range of poisonings other than paracetamol. The scientific basis for the treatment is, however, scarce - especially concerning human data. As the poisonings in question are rare we might here have a subject suitable for multi-national studies. *References:* 1. Locatelli C, Butera R, et al. 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128. The Evaluation of Standard Medical Terminology Systems to Describe Symptoms of Poisoning, an Output of the ASHTII Project

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Introduction: An Alerting System for Chemical Threats (ASHTII) is currently under development to improve the speed and effectiveness of detection, evaluation and public health response to accidental and deliberate chemical release. This alerting system will deliver an approach allowing different levels of access by the creation of a European Union Poison Centre Forum (EUPC Forum) to enable poison centres to communicate with each other and a Rapid Alert System for Chemical Health Threats (RAS-CHEM) for national public health authorities and health ministries to communicate events that may have a potential public health impact (either nationally, cross-border or internationally). A fundamental requirement for the EUPC Forum and RAS-CHEM to operate successfully (in an interdisciplinary multi-language environment) is to adopt standardised terminology to describe clinical effects in both systems. *Methods:* A literature review of symptoms associated with exposure to relevant chemicals was undertaken; this included chemicals that have a high risk of accidental or deliberate release and chemicals of interest to poisons centres. Clinical Effect Profiles (CEPs) were produced to provide concise tabulated summaries of clinical effects reported in the available literature. All clinical effects identified in the review were compared to symptoms reported in internationally standardised terminology systems such as MedDRA, SnoMED-CT, WHO-ART and poison centre specific terminology such as NPDS and GFKT. *Results:* From the 118 chemical agents included in the literature review, 1011 clinical effects were identified. 108 individual CEPs were produced; seven were grouped as 'organophosphates' and three as 'cyanides'. *Conclusion:* In the development of the alerting system it is intrinsically important that both the EUPC Forum and RAS-CHEM can capture the wide spectrum of clinical effects associated with toxic chemical exposure and poisonings. The use of a limited terminology system containing broad definitions of clinical effects may result in reduced sensitivity of the alert system. As a result an internationally standardised terminology system such as MedDRA or SnoMED-CT has been recommended for inclusion in EUPC Forum and RAS-CHEM. The terminology system chosen for alert systems may become a basis for collation or exchange of cases from poisons centres for different purposes in the future.

129. Further Development of the Alerting System for Chemical Health Threats, Phase II (ASHTII)

Wyke S,[1] Orford R,[1] Duarte-Davidson R,[1] Desel H,[2] Schaper A,[2] Pelclova D,[3] Mathieu-Nolf M,[4] Edwards N,[5] Sutton N,[5] Kennedy K,[5] Tizzard Z,[5] Dragelyte G,[6] Good AM,[7,9] Kupferschmidt H.[8,9]
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Objective: The aim of the Alerting System for Chemical Health Threats - Phase II (ASHTII) project is to improve the speed and effectiveness of public health response to toxic exposures following deliberate or accidental chemical incidents or emergencies. *Background:* Currently there is no standardised format or protocol for sharing information or issuing alerts about chemical incidents throughout EU Member States. To address this concern, the European Union Public Health Programme funded a project that demonstrated poison centres are a feasible resource to detect sentinel events and established the concept of a Rapid Alert System for CHEMical health threats (RAS-CHEM) (ASHT Phase I). Recommendations from ASHTI have been taken forward in ASHTII to develop a communication system able to operate as a rapid Alerting System for chemical Health Threats (ASHTII). *Discussion:* RAS-CHEM will be extended to allow different levels of access to the system by the creation of a European Union Poison Centre (EUPC) Forum that enables Poison Centres to communicate with each other directly. RAS-CHEM will be reserved for national public health authorities and health ministries to communicate events that may have potential public health impact (either nationally, cross-border or internationally). For both facets of the rapid alert system to operate successfully standardised terminology has been recommended for inclusion in both the EUPC Forum and RAS-CHEM, both to describe clinical effects and classify chemical agents. User protocols are also being developed. *Conclusion:* The range of mechanisms that already exist for reporting chemical health threats in ASHTII project partner EU Member States has been established, and RAS-CHEM is due to undergo extensive testing with ASHTII associate and collaborating partners and external stakeholders. RAS-CHEM is viewed as a practical and valuable addition to the European Union and the Health Emergency Operation Facility (HEOF).

130. New Zealand and Australian Emergency Department Sources of Poisons Information

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Objective: The New Zealand National Poisons Centre has developed a comprehensive poisons information database - TOXINZ - utilised by the majority of New Zealand

Table 1. New Zealand and Australian emergency department sources of poisons information

	Daily	Weekly	Monthly	Yearly	Never	No Answer
Refer to an electronic poisons information database #						
New Zealand	29%	55%	12%	4%	0%	0%
Australia	8%	30%	22%	16%	16%	8%
Use in-house protocols *						
New Zealand	20%	33%	20%	8%	18%	0%
Australia	30%	41%	24%	5%	0%	0%
Refer to a textbook *						
New Zealand	0%	8%	33%	16%	33%	10%
Australia	3%	30%	24%	11%	14%	19%
Ring a Poisons Centre *						
New Zealand	0%	2%	14%	57%	27%	0%
Australia	0%	8%	38%	30%	24%	0%

#$p < 0.01$, *$p < 0.05$ Chi squared, Fisher exact test

emergency departments. This resource has not been formally made available in Australia, where the primary electronic poisons information resource is Poisindex®. This study was designed to identify if availability of TOXINZ in New Zealand has caused differences between New Zealand and Australian emergency departments in their level of use of electronic, and other, poisons information resources. *Methods:* A preliminary survey tool was developed and presented to staff in one emergency department for comment and validation. Following revision, six emergency departments in both New Zealand and Australia each received ten of the resulting questionnaires - a total of 60 to each country. The survey was commenced on 14 April 2008 and closed on 30 June 2008. *Results:* The survey achieved an 81.67% (n = 49) and 61.67% (n = 37) response rate in New Zealand and Australia respectively. Seventy per cent of New Zealand and 86% of Australian responders were doctors, with the remaining replies from nursing staff. Key results are outlined in Table 1. New Zealand responders had a highly significant ($p < 0.01$) preference for the use of an electronic poisons information database, and Australian responders a significantly ($p < 0.05$) increased reliance on in-house protocols, textbooks and use of a Poisons Information Centre. *Conclusion:* The availability of TOXINZ in New Zealand influences a preference for the electronic form of poisons information when compared to Australia, where TOXINZ is not formally available.

131. The Use of Record Based Markers to Evaluate the Quality of Documentation of Inquiries to the Danish Poison Information Centre. An Audit Procedure

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Objective: The Danish Poison Information Centre (DPIC) offers poisoning advice to health professionals and the general public by telephone. Calls are answered by nurse specialists with backup from physicians specialised in occupational and environmental medicine, clinical pharmacology and anaesthesiology. All calls are registered in a database using a structured record that serves different purposes: 1. Collection of relevant data to undertake a correct and consistent individual risk assessment, including an evaluation of when to seek backup from the physician on duty. 2. A proper documentation of the sequence of events. 3. An active detection and validation of adverse events related to toxic exposures (toxicovigilance). The purpose of the present audit is to evaluate the quality of documentation using record-based markers. *Methods:* The DPIC`s local quality board identified 16 "quality-markers" within the DPIC record using the concept of face-validity. These markers concerned the following areas 1. Identification of the exposure, the exposed person and the caller. 2. Record of toxicological symptoms and vital parameters. 3. Description of event, risk assessment and given advice. 4. Local guidelines for the management of the poisoning in question. Four monitors, two physicians, one pharmacist and one nurse, evaluated a total of 200 DPIC records, 100 drug-intoxications and 100 environmental exposures, randomly chosen from the DPIC database. *Results:* In thirty-nine cases (19.5%) the exposed person was not clearly identified. This includes three cases where the caller requested anonymity, and 15 cases where the identification was judged to be irrelevant by the monitor. In ninety-four cases (47%) the exposure (time, amount and/or type of poison) was unclear. In ninety-five (46%) cases toxicological symptoms were not recorded. In thirty-seven cases (23%) the sequence of events and in five cases (2.5%) the given advice were ambiguous. In sixty-five cases (32%) no local guidelines existed. *Conclusion:* The presented audit procedure is a valuable tool to detect shortcomings in the documentation of inquiries to the DPIC. While some are difficult to influence, e.g. limited information of toxic exposure, others, e.g. ambiguous advice, must be areas for a targeted effort, to ensure the necessary quality of toxicological advice and use of data for toxicovigilance.

132. A Research Program at a Small- to Mid-Sized U.S. Poison Center

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Background: Poison centers perform many functions, among them management of acute poisonings; public and professional education; regional and national toxicosurveillance; and research. The organizational structure and economics of small- to medium-sized poison centers, however, pose challenges to the development of a research program. The New Mexico Poison and Drug Information Center (NMPDIC) is a small- to mid-sized U.S. center, serving a population of 2.5 million and receiving about 45,000 calls per year. Over the past decade, it has had between 1 and 2 medical toxicology full time equivalents (FTEs), a Diplomate of the American Board of Applied Toxicology (DABAT)-certified managing director, a two-year pharmacy toxicology fellowship (one fellow per year), 10 poison specialist FTEs, and one administrative assistant. The poison specialist job description does not include a research role. *Objective:* The purpose of this presentation is to characterize the research program developed at the NMPDIC and its methods of overcoming these obstacles. *Research program:* The NMPDIC has developed a research program which consists of funded research, no-direct-cost NPDS database analyses, participation in multicenter clinical trials, pharmacy fellow research projects, collaboration with researchers in other university departments, and volunteer efforts of poison specialist staff. *Research output:* Between 2000 and 2009, the NMPDIC has published 49 peer-reviewed, scientific manuscripts, including 22 retrospective case series (16 involving analysis of multi-center or national databases and six as single-institution analyses); 12 case reports; 1 review article; 10 original research manuscripts (6 related to clinical trials or practice; 2 post-mortem studies; and 2 basic science studies); and 4 other peer-reviewed manuscripts. In addition, there were 45 published scientific abstracts, most presented at national or international scientific meetings. *Discussion:* Despite limited personnel, protected research time, and financial and other resources, the NMPDIC has been able to create a multifaceted research program which has brought in external research funds and generated academic output including participation in randomized, prospective clinical trials, clinical and basic science investigations, epidemiologic studies, and retrospective case series and reports. *Conclusion:* A vigorous, multi-faceted research program can be developed despite limitations of staff, time, and resources.

133. Mercury Enquiries to a National Poisons Information Centre - Poisoning or Exposure?

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Objective: Public awareness of the potential of mercury to cause health problems and the need to avoid unnecessary exposure has increased in recent years. As a result of this publicity, members of the public may ascribe unusual neurological symptoms and signs to mercury 'poisoning'. This study was performed to audit exposures to mercury and resulting toxicity. *Methods:* All telephone enquiries, over a 57 month period, to the National Poisons Information Centre (NPIC) were retrospectively reviewed. Only calls between 8 am and 10 pm were included in the study. *Results:* 258 enquiries regarding mercury in all its forms were recorded by the NPIC over the study period. 132 (51.1%) were calls received from members of the public, 72 (27.9%) were from general practitioners and primary care out-of hours services and 54 (21.0%) were from hospitals. In cases where human exposure occurred (n = 191), 104 (54%) patients were children (<16 years) and 87 (46%) were adults. Enquiries regarding metallic mercury in mercury thermometers accounted for the majority of calls (n = 185). These included enquiries after accidental mercury ingestion from thermometers (n = 116), information on clean-up procedure after mercury thermometer breakage (n = 59), skin contact after mercury thermometer breakage (n = 6) and inhalation of mercury after mercury thermometer breakage (n = 4). In the patients who were exposed after ingestion of mercury from thermometers, 112 reported no symptoms and 4 had reported vomiting. Information on clean-up procedure after sphygmomanometer and barometer breakage accounted for 12 enquiries. Enquiries about potential toxicity from dental amalgams accounted for 21 calls and exposure to mercury after breakage of Compact Fluorescent Lamps (CFL) bulbs accounted for 6 calls. NPIC received 2 calls about patients with mercury toxicity. One patient was already receiving chelation therapy, and the other was a patient looking for chelation therapy after being diagnosed with mercury toxicity in a private clinic. *Conclusions:* The majority of enquiries received by the NPIC during the study period were about accidental ingestions of metallic mercury from thermometers in children. This usually occurred when the child bit on the thermometer. Significant exposure to mercury was infrequently encountered.

134. Status and Trend in the Total Top-10 of Inquiries to the Danish Poison Information Center

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Objective: Status and trend in the Top-10 of inquiries to the Danish Poison Information Center (DPIC), a public and health personnel 24h-telephone service. We

investigated if a year-based DPIC Top-10 can provide reliable specific information on poisoning trends, and new and upcoming poisonings in Denmark. *Methods:* All inquiries to DPIC from health personnel and citizens in Denmark were sorted by whole years (2007 and 2008) and the first nine months in 2009. Only inquiries with a prevalence of at least 5/year were included. The inquiries were divided into 18 main groups, each with 10–20 subgroups. *Results:* Top-10 of the 18 main groups are presented as per cent of the included number of inquiries. Year 2007: Household products (16%); Chemicals, other (10%); Weak analgesics (10%); Plants (9%); Pharmaceuticals, other (8%); Anxiolytics (8%); Antidepressants (6%); Drugs of abuse (6%); Antipsychotics (5%); Alcohol (4%). Year 2008: Household products (18%); Weak analgesics (11%); Plants (10%); Pharmaceuticals, other (7%); Chemicals, other (7%); Antipsychotics (7%); Drugs of abuse (6%); Antidepressants (6%); Anxiolytics (5%); Vitamins (4%). First nine month of 2009: Household products (18%); Plants (15%); Chemicals, other (10%); Weak analgesics (10%); Pharmaceuticals, other (6%); Anxiolytics (5%); Vitamins (5%); Antipsychotics (5%); Antidepressants (5%); Drugs of abuse (4%). In general, drug poisonings account for approximately 40% of the included inquiries and the weak analgesics (paracetamol, NSAID, salicylic acid) constitute one eighth of all inquiries. Furthermore, vitamin-containing products entered the Top-10 in 2008, and increases. *Conclusion:* A specific detailed list, and an organised database and data materials are necessary to notice changes in poisoning patterns. The rise of inquiries concerning vitamin-products occurred in 2008 and continues rising in 2009. This might be correlated to new palatable, eye-catching, easy access products for kids. The results emphasize the importance of a fine-meshed grid and correct registration in a national poison information center if increase in new specific poisonings is to be noticed. Consequently relevant information to the national public administration and healthcare system can be provided in time to: 1) provide early detection of poisoning trend changes, 2) prevent further escalation in number of a potentially dangerous specific xenobiotic poisoning.

135. Health Care Disparities in Delivering Poison Center Services to Spanish Speakers in Texas

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Objective: Spanish speakers make up the second largest language population group in the United States of America. The largest numbers of this ethnically diverse group reside in the states of California and Texas. Use of poison center call services by the Spanish speaking population of Texas is significantly low, but this health care disparity has not been well characterized. To better describe this underutilization, we studied the correlation between calls received from Spanish-speaking callers by the six poison centers that comprise the Texas Poison Center Network (TPCN) and the total volume of calls received. Data will be used to help regional poison centers better serve constituent callers whose primary language is Spanish. *Methods:* Call center data was evaluated from 2001 through 2008 to determine the number of calls received from Spanish speakers by each of Texas' regional poison centers. All Spanish language calls were examined to determine the degree of correspondence, if any, between the region from where calls originated versus the region at which the calls were handled. *Results:* Over the eight-year study period, Texas regional poison centers received 2,607,151 calls. Of these, only 29,151 (1.12%) were handled in Spanish, originating from the following centers: Texas Panhandle (671), Central Texas (1,951), North Texas (5,226), West Texas (6,602), South Texas (6,939), and Southeast Texas (6,951). Of all Spanish-language calls, the South Texas and West Texas Poison Center handled 83.34%. This was shown partly to be due to a larger proportion of these calls originating in the regions served by these two centers, as well as calls purposefully transferred to them because they are staffed by bilingual (Spanish/English) call-takers. *Conclusion:* This evaluation of calls received by Texas poison centers demonstrates a major language-based disparity in call center utilization, showing only 1% of calls generated from the Spanish-speaking population. This evaluation provides the foundation for greater efforts to be used towards educating this community on the services provided by poison centers. To more effectively provide regionalized care to this population, call volume must be reflected in adequate bilingual call-taker staffing in regions with significant populations of Spanish speakers.

136. Anticipating the Forthcoming European Harmonisation a New Product Notification Procedure was Introduced: Lessons Learned

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Objective: To describe a new notification procedure in the Netherlands. *Methods:* Although obligatory, the notification of dangerous products to the Dutch Poisons Information Centre (PIC) has never been satisfactory. Industry complained both about the required quality of the information and about the required format. In revitalising the product notification process, the Dutch PIC and the industry reached new agreements on the quality, the format and on the notification procedure. *Results:* As notification of a complete composition is required by the detergents regulation (EC No 648/2004) in order to inform physicians appropriately, the notification of all ingredients in a product to the Dutch PIC was no longer a problem for the Dutch industry. In addition, defined concentration ranges (EAPCCT guideline, newsletter April 1996) for all ingredients as minimum requirements, turned out to be acceptable for the industry. The required information on the composition and concentrations is not present on a Safety Data Sheet (SDS), and thus has to be separately notified together with an SDS. The SDS can serve as a basic format. Currently, it mostly contains minimal information on the toxicological properties of the dangerous product, but this will improve with the forthcoming new SDS requirements (in 2010 for substances, in 2015 for mixtures) in the REACH Regulation (EC No 1907/2006). Industry readily accepted submission of these two documents, especially, when an easy upload of the product information through a secure website was possible. In the first six months 6400 products were notified, as many as was notified in the thirteen years before! The processing of the submitted information is almost completely automatic with few manual tasks for the PIC. This is beneficial to PICs with limited financial resources. *Conclusion:* The Dutch PIC developed a flexible product notification procedure, anticipating European harmonisation as intended by article 45(4) of the EU-GHS Regulation (EC No 1272/2008). Lessons learned are: 1) discussions mainly concerned the required ingredient concentration (exact concentrations or defined ranges), 2) accepting the SDS besides a detailed product composition was welcomed by industry increasing the willingness to notify and 3) product information can be adequately processed and made available for Poisons Information Service with a minimum of manual labour.

137. Study of the Reliability of a Poisoning Severity Score "PSS": Moroccan Poison Control Centre Experience

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Objective: To assess the reliability of the poisoning severity Score (PSS) through a prospective study in two Toxicology units (toxicological information unit and toxicovigilance unit) of the Moroccan Poison Control Centre (MPCC). *Methods:* Study of the reliability of PSS involved 200 observations (100 files received from the toxicological information unit and 100 files from the toxicovigilance unit). We included all observations containing information essential for the gradation of PSS, notably the symptomatology and the final outcome of the patient. This study was conducted by 3 operators who are physicians with experience ranging from 2 to 4 years. For grading the physician used PSS.[1] The study of concordance between gradation performed by the different operators was evaluated by the kappa test: kappa = 0: total discrepancy; kappa = 1: perfect concordance; kappa <0.40: poor concordance; 0.40 < kappa <0.75: satisfactory concordance; kappa > 0.75 very good concordance. *Results:* The study on the general concordance between the 3 operators has produced a satisfactory kappa (kappa = 0.81). The Kappa was 0.83 for files of toxicological information and 0.79 for files of toxicovigilance. The study of concordance according to the toxic class is illustrated in Table I. *Conclusion:* The PSS is a reliable tool for evaluating the severity of poisoning. This score, based on relatively basic data, is particularly useful for poison control centers. The improvement and refinement of this score is influenced by more frequent use by practitioners and especially with a critical eye. *References:* 1. Persson HE, Sjöberg GK, Haines JA, et al. Poisoning Severity Score. Grading of Acute Poisoning. Clin Toxicol 1998; 36:205–13.

Table 1. Results of concordance according to the toxic class

Toxic class	Effective	kappa
Drugs	68	0.74
Gas	30	0.27
Pesticide	25	0.78
Industrials product	25	0.81
Food	18	0.77
Household product	13	0.82
Venomous animal	11	0.28
Plants	10	–

138. Model for Rationalisation of Antidote Stock Holding in Hospitals

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Objective: To present a model for organising and rationalising hospital antidote stockholding within regional districts. *Methods:* Following published guidelines by the British Association of Emergency Medicine on Antidote Availability in Accident and Emergency Departments in June 2006,[1] NPIS (Newcastle) undertook a survey of hospital antidote holdings within the north of England. In response to this survey and updated guidelines by the College of Emergency Medicine (CEM) in May 2008,[2] the Medicines Information (MI) Service at Leeds Teaching Hospitals NHS Trust resurveyed Yorkshire hospitals via the UKMI network of pharmacists. NPIS (Newcastle) was then contacted for advice regarding the CEM guidelines and recommendations for stock holdings, particularly in relation to rarely used and/or expensive antidotes. A proposal was prepared for consideration by the Yorkshire Chief Pharmacists Group, which suggested specific placement of antidotes around the region enabling access within an acceptable time period and also facilitating shared financial burden of expired stock. *Results:* NPIS (Newcastle) received 22 responses from 62 hospitals surveyed (35%). From the Yorkshire region 7 responses from 14 hospitals were received (50%). Following resurvey, responses were received from 14 of 16 Yorkshire hospitals (87.5%). Discussions between NPIS (Newcastle) and the MI Service related to the following antidotes: phentolamine, cyanide antidotes, fomepizole,

pralidoxime, viper and other antivenoms, Prussian Blue, DMPS and DMSA. Specific issues considered were transport times from stock holder to patient, quantities to stock and availability of supraregional supplies. The proposal prepared for the Chief Pharmacists Group has been well received and broadly supported, with the suggestion to develop a standard operating procedure to be followed by all Yorkshire hospitals when obtaining an antidote through another hospital within the region. *Conclusions:* Cooperation between hospitals within regional districts and advice from a poisons service can achieve rationalisation of antidote stockholding. *References:* 1. British Association of Emergency Medicine. Guideline on Antidote Availability for Accident and Emergency Departments [Online]. 2006 June [cited 2009 Oct 31]. Available from: http://www.collemergencymed.ac.uk/CEC/Antidote_list_June_2006-Summary.pdf 2. College of Emergency Medicine. Guideline on Antidote Availability for Emergency Departments [Online]. 2008 May [cited 2009 Oct 31]. Available from: http://www.collemergencymed.ac.uk/CEM/Clinical%20Effectiveness%20Committee/Guidelines/Clinical%20Guidelines/

139. Preparedness for Chemical Emergencies: A Survey About Training Needs Of Italian Emergency Medical Department Staff

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Objective: To investigate training needs in chemical emergencies of Italian emergency medical and nursing staff. *Methods:* A questionnaire was distributed in 2007–2009 to health emergency personnel enrolled during 24 toxicology courses all over Italy. The questionnaire, given before the course began, was composed of ten questions aimed to investigate (i) knowledge about diagnosis and antidotal treatment of some toxidromes in chemical emergencies, (ii) availability of NBC individual protection devices (DPI) and devices for decontamination, and the ability to use them. *Results:* Among 504 returned questionnaires, 4 were excluded for incompleteness of data and 500 were included for the evaluation: 356 (72.2%) were filled in by physicians and 144 (28.8%) by nurses. Physicians and nurses enrolled in the survey were working in out-of-hospital Emergency Medical Services (89/500, 17.8%), in hospital Emergency Departments (315/500, 63%), in Intensive Care Units (60/500, 12%) and in other hospital departments (i.e. general medicine, surgery) (36/500, 7.2%). Results of selected items regarding antidotes/toxidromes and DPI are reported. The clinical use for amyl nitrite was unknown by 61.2% (306/500) of all the interviewees, by 55.9% of the physicians (199/356), and by 74.3% of the nurses (107/144). 58.6% (293/500) of the interviewees [50.28% of physicians (179/356), and 79.16% of nurses (114/144)] did not know the diagnostic role of plasma acetylcholinesterase in nerve agent poisoning. 75.8% (379/500) of those interviewed gave an incorrect answer about blood-gas-analysis alterations in cyanide poisoning. 85.6% (428/500) of those interviewed had never worn individual protection devices. *Conclusions:* The data collected reveal a lack of preparedness for major chemical emergencies: this may be related to the rarity of NBC major events and to the rapid turn-over of medical and nursing staff in Italian emergency services. Poison centers may play a key role in continuous and specific training in this area. *Acknowledgements:* Study carried out with the support of Italian Civil Protection Department.

140. Surrogate Markers for Swine Flu using TOXBASE® - Antivirals, Cough and Cold Preparations

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Objective: To investigate surrogate markers for H1N1 (swine flu). *Methods:* Enquiries to Poisons Centres in the US have been used to track spread of infectious disease (NPDS report 2008 in press). TOXBASE® is the Internet poisons database used by health professionals in the UK for managing poisoned patients. An increase in influenza cases might be expected to see a corresponding increase in TOXBASE® enquiries concerning pharmaceutical products used in treating the symptoms. In the UK at the height of the initial epidemic diagnosis was available by telephone and oseltamivir and zanamivir were provided without confirmation of the virus. Monthly TOXBASE® accesses from England and Wales for the period 1/1/2009 to 31/10/2009 were reviewed for oseltamivir, zanamivir, cough and cold preparations (relevant pharmaceutical preparations containing "cold", "flu", "cough" or "throat" in the product name), paracetamol and ibuprofen. Weekly figures for antiviral accesses were compared with estimated GP consultations/100,000 population for flu in England and Wales for May-October 2009.[1] *Results:* Oseltamivir had an average of 1.7 accesses/month and zanamivir 0.7/month for the period Jan 2006-April 2009 and thereafter registered 1007 and 70 accesses respectively in the following six months, with peaks of 460 and 36 in July 2009. Cough and cold preparations accesses (mean 727; range 276–1908) showed seasonal variation with peaks (> 1000 accesses) in Jan and Mar 2006, Feb and Dec 2007 and Dec 2008, but no peak in July 2009. Ibuprofen showed little variation with a mean number of accesses of 3116 (range 2692–3709). Paracetamol accesses varied over the period with little pattern (mean 7375; range 6156–9330). Since TOXBASE® enquiries concerning antivirals did appear to mirror swine flu the weekly numbers were compared with GP influenza referrals. GP referrals peaked in the week ending 19 July and TOXBASE® accesses peaked 1 week later. *Conclusion:* Accesses to antivirals showed a distinct peak, which followed by one week the peak in the estimated number of influenza referrals. These may provide a rapid confirmation of medicine uptake in the population and disease spread. In contrast cough and cold preparations, paracetamol and ibuprofen containing products did not provide surrogate markers in the UK. *References:* 1. http://www.hpa.org.uk/HPA/Topics/InfectiousDiseases/InfectionsAZ/1242949541993/ accessed 10 Nov 2009.

141. The French Toxic Exposure Surveillance System: Adaptation of a Business Intelligence System for Toxicovigilance

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Objective: The French Toxic Exposure Surveillance System (F-TESS) has 2 goals: 1) to help physicians in their daily work; 2) to contribute to toxicovigilance. In the context of this second objective, medical data produced by F-TESS are analyzed by a business intelligence system in order to detect potential new problems, to monitor on-going studies, and to perform quality control. *Methods:* Since 2000, a structured medical file is filled out for each call received by a French poison centre. These files are consolidated daily into the French National Database of Toxic Exposures (FND-TE). This database and the French National Database of Substances and Products (FND-SP) are constantly evolving; both are stored in a Data Warehouse. A Business Intelligence system allows authenticated users to perform queries and statistical analyses on the data collected. A very good performance is obtained due to precomputed indicators. *Results:* National and regional toxicovigilance surveys are performed and followed by creating a specific query and scheduling automatic execution at the required frequency (daily, weekly. . .). People in charge of these studies automatically receive notification emails after each execution. This tool can also provide signal analysis for epidemiological studies. Significant increases of exposure to specific products or classes of products, and newly observed reactions to specific substances are two examples of current fields of research. Quality control is also performed on all data in various ways. Cross-data analysis may identify any inconsistencies. Retrospective evaluation of randomly selected files is systematically performed to improve coding. Automatic queries can also be run to identify quality indicators and monitor their evolution. *Conclusion:* The use of modern data warehousing and business intelligence solutions allows intelligent access to collected data, allowing automatic analysis, signal generation and quality control with a potential to significantly improve knowledge in the field of toxicological epidemiology.

142. How Long Does it Take to Document a Call to a Poison Center?

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Objective: Electronic written documentation of calls is the standard in all U.S. poison information centers. A retrospective observational study was conducted at an AAPCC certified regional poison information center to determine the amount of time required to conduct the initial documentation of both exposure and information calls and whether the length of time to perform the documentation of exposure calls was influenced by either the ultimate outcome (severity) of the patient or the reason for the exposure. *Methods:* The Visual Dotlab Enterprise (WBM Software, Fresno, CA; release 4.3.7, 2009) was utilized by the poison information center to document all exposure calls. The software has an integrated timing component that tracks all entries. Data from records that were collected from January-September, 2009 that contained no specific patient identifying information (mean and median length of time [minutes] to complete the initial documentation, reason for the exposure and outcome) were downloaded from the medical record system to a relational database for analysis. Descriptive statistics were utilized to characterize the data. *Results:* During the study period, 47,041 exposure (32,665) and information (14,376) calls were documented electronically. Exposure calls required more time (mean 4.14 minutes; median 2.10 minutes) than information calls (mean 1.71 minutes; median 0.30 minutes) to complete the initial documentation. The mean time to document all calls initially was 3.40 minutes (median 1.50 minutes). Definitive outcome information was documented on 7,777 of the records. The means/medians (minutes) were: no effect 4.96/2.80; minor effect 5.81/3.40; moderate effect 6.60/4.50; major effect 7.68/4.80; fatality 6.80/4.95. Nineteen reason categories were documented among the exposure calls. Examples of those results included: unintentional/general-mean 3.29 minutes (median 1.6 minutes); intentional/suspected suicide-5.92 minutes (median 3.95); adverse reaction/drug-9.10 minutes (median 4.80). *Conclusion:* Specialists in poison information are efficient in the initial documentation of calls to a poison center. The length of time to complete the electronic documentation was in direct relationship (longer time associated with greater severity) to the severity of the ultimate outcome. Unintentional (accidental) exposures required less time to document the initial note than exposures that were intentional and for adverse drug reaction calls.

143. Identification and Characterization of Surges in Poison Center Call Volume

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Objective: High volume surges in health care demand are rare, unpredictable events, making their impact on health system performance and surge capacity difficult to study. We aimed to explore methods of identifying time periods with surge-like conditions at a US poison center and to determine whether cases during these periods are different from non-surge periods. *Methods:* Incoming

call data from a US poison center over twelve consecutive months was collected via a call logger and an electronic case database (Toxicall). Variables indicative of surge-like conditions included in-call duration, number of cases and number of calls per staff member per 30-minute period. Using maximum likelihood estimation, six probability distributions (Exponential, Gamma, Weibull, Chi squared, F, Normal) were evaluated for each variable to determine best fit for identifying unusually high levels of staff call activity. Surge-like periods were defined *a priori* as busier than 99% of all other 30-minute periods and non-surge as slower than 70% of all other 30-minute periods. Case characteristics and distribution of surge-like and non-surge calls were compared using logistic regression and odds ratios. *Results:* A total of 65,364 incoming calls occurred over 12 months. The Weibull distribution was the best fit for the calls per staff and cases per staff variables. The Gamma distribution was the best fit for in-call duration. One hundred (0.6%) surge-like and 4885 (27.8%) non-surge 30-minute periods were identified. Calls during surge-like periods were more likely to involve patients less than 6 years old (OR 1.6, 95% CI 1.20, 2.16) and less likely to be intentional exposures (OR 0.7, 95% CI 0.51, 0.97). There was no difference in route of exposure, number of substances per case, or clinical outcome between surge-like and non-surge period cases. Surge-like periods were more common at 1000, 1100 and 1800 hours; on Mondays, Wednesdays and Saturdays, and during the winter months. *Conclusion:* A method for identifying periods of surge-like activity for poison center incoming calls was demonstrated. This allowed comparison to non-surge periods for call characteristics. Staffing patterns, communication, and program capacity can be evaluated using this process in planning for larger call volume surges during disasters.

144. Unexplained Lactic Acidosis and Toxicological Performance in Non-poisoned Patients

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Objective: Physicians may call the Poison Centre for advice in the diagnosis and management of critically ill patients with unexplained lactic acidosis. In a short time frame, we were consulted for two such patients, described here. *Case series:* 1. A 75-year-old woman was admitted to the medical ICU for abdominal pain and hyperventilation. ECG and routine laboratory tests were within normal limits. Arterial blood gases revealed pH 6.78, pCO_2 11 mmHg, pO_2 150 mmHg and HCO_3 4.2 mmol/L. Lactate levels were increased (11 mmol/L, normal range 0.5–1.6 mmol/L). Elevated anion gap of 20.5 mEq/L (normal range 8–12 mEq/L) and increased osmolar gap of 17.4 were present. The patient was not diabetic, and denied any alcohol abuse or drug therapy. IV infusion of sodium bicarbonate 100 mmol did not improve acidosis. Poison Control Centre was called to rule out methanol or ethylene glycol poisoning. In the meantime, vitamin B1 100 mg was administered three times and lactate levels decreased to 7.1 mmol/L. The patient's condition improved with resolution of symptoms 12 hours later. The patient's relatives admitted that the patient had a congenital thiamine deficit. 2. A 40-year-old pregnant woman at the 27th week of pregnancy was admitted to the obstetrician unit for abdominal pain and hyperventilation. The patient was not diabetic, and denied any abuse or drug therapy. She complained of vomiting for several days. Arterial blood gases revealed pH 7.4, pCO_2 27.4 mmHg, pO_2 101.4 mmHg and HCO_3 17.4 mmol/L. Lactate levels (5.2 mmol/L) and anion gap (13.8 mEq/L) were increased and ketonuria 2+ to 3+ was present. Diagnosis of diabetic ketoacidosis was rejected because of the glucose level (83 mg/dL) and a normal glucose tolerance test. Poison Control Centre was consulted because of suspected salicylate poisoning, but toxicological analysis was negative. Intravenous fluids and antiemetic treatment resolved patient's symptoms and she was discharged the day after with normal lactate levels (1.4 mmol/L) and diagnosis of late hyperemesis gravidarum. *Conclusion:* Poison Centre staff has to be familiar with the differential diagnosis of metabolic acidosis, since toxicological advice may be required before other evaluations have been completed, even in those patients with a history clearly negative for poisoning.

145. Mushroom Toxicity: Impact of Fungi with Unknown Toxicity, Data from a Prospective Half Year Survey in One Poison Control Centre

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Objective: Poison Control Centres (PCC) frequently receive inquiries concerning human exposure to mushrooms. According to US-American TESS-data, the vast majority of these cases are coded as generic with no further identification of the mushroom. Obviously in these cases the toxicity of the mushrooms is not known. However in many of such cases, even if the fungus were identified, no risk assessment would have been possible, due to lack of toxicological data of the species. Future investigations should address the clinical course after ingestion of those identified mushrooms with unknown toxicity (MUT). In Germany a network of certified mycologists (CM) exists which can help local health care facilities in identifying fungi. Their contact data are available to PCCs in their own data base. Future investigations, therefore, should be performed by PCCs with the help of those mycologists. This preliminary study is done to estimate the presumed number of mushroom ingestions with identified MUT. *Methods:* Data were collected prospectively in Munich PCC (serving 12 million inhabitants, 33,000 calls/year) from all cases with ingestion of wild mushrooms, excluding those purchased from the food trade during April - October 2009: number of calls with identified mushrooms, consultations with CMs, number of ingestions of MUT. Toxicity was assessed by a CM (B.H.) into classes: highly toxic (HT), low toxicity (LT), edible, edible but known for adverse reactions in individual cases (EAI), not able to be assessed, and MUT. Two hundred and forty-six cases met the inclusion criteria, 80 cases had mushrooms identified, in 74 a CM was consulted. 15 cases had eaten 8 different HT species, 18 cases LT species, 14 cases EAI species, 18 cases had eaten 11 MUT species. From these, 6 cases reported minor symptoms after ingestion of 4 species. *Results:* In this survey we registered 18 cases of ingestions of 11 mushroom species with unknown toxicity. *Conclusion:* For further investigations assessing the effects after ingestion of mushrooms with unknown toxicity counselling by certified mycologists will be useful but only a few cases which can be evaluated can be expected. A cooperative data collection by multiple PCCs in a shared database will be valuable.

146. Geographic Information System Mapping of Poisoning Cases in North Palestine

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Objective: To utilize the Geographic Information System (GIS) technology to study the different types of poisoning among citizens in Nablus governate, north Palestine. *Methods:* All patients admitted at Al-Wattani hospital due to poisoning during a 12-month period were included. The study started in May 2008 and ended in June 2009. All data were entered and analyzed using SPSS program. Maps were drawn using the Arc GIS 3.2 program. *Results:* A total of 674 poisoned patients from different geographical areas were admitted to Al-Wattani hospital during the study period. The patients were of different age groups and were exposed to different agents. The most commonly encountered agents were biological (77.4%) and chemical (23.1%). Most cases resulted from accidental exposure; however, there were 8% that resulted from intentional behavior. GIS localization of poisoning revealed that it is randomly distributed in Nablus district with more occurrences toward south and south east areas. Biological poisoning mainly occurred in Nablus city and in the southeastern area of its suburbs, an agricultural area that is known for farming. The GIS shows that chemical poisoning is more localized toward the northern area of the governate. Finally, GIS mapping revealed that suicidal poisoning is occurring mainly to the east of Nablus, mainly in a refugee camp known as Askar. *Conclusion:* There is more biological poisoning in the agricultural areas and more suicidal poisoning in the refugee camps. This mandates decision makers to take appropriate action in this regard.

147. Epidemiology in Acute Poisoning in Children - One Year Comparative Study in Two Pediatric Poisoning Centres

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Objective: To compare the structure, management and evolution of poisonings in two pediatric poisoning centres. *Methods:* We have performed a one year retrospective study in two pediatric poisoning centres in Romania: Pediatric Poisoning Centre "Grigore Alexandrescu" Hospital Bucharest and Pediatric Poisoning Centre "Sfinta Maria" Hospital Iasi. *Results:* See Table 1. All the acute poisonings reported between January 1st - December 31st 2008, were studied taking into consideration: age, gender, residence, etiology, modality of producing, consciousness status, gastric lavage, antidote administration, deaths. There are some differences regarding the structure of poisoning between the two centres: in Bucharest more cases with carbon monoxide (CO) (from individual heating stations) while in Iasi acute methemoglobinemia is more frequent (nitrites from well water). Gastric lavage was performed more frequently in Iasi compared to Bucharest (In Bucharest the EAPCCT protocol for gastro-intestinal decontamination is more strictly applied). A bigger percentage of poisonings benefited from antidotes in Bucharest (problems with antidote supplies in Iasi). More unknown substances reported in Iasi (difficulties in performing toxicology analyses). *Conclusion:* Even if the structure of acute poisoning is quite similar between the two centres there are many differences due to social and economic conditions in the two regions and administrative organization. *References:* 1. Tempowski J. Epidemiology of Poisoning in Children. In: Bates N, Edwards N, Roper J, et al, eds. Paediatric toxicology: handbook of poisoning in children. London, England: Macmillan Reference Limited, 1997:1–5.

148. Paracetamol (Acetaminophen)-Related Deaths Reported to United States Poison Centers: Paracetamol Single Ingredient Products and Paracetamol-opioid Combination Products

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Objective: A US Food and Drug Administration Advisory Committee recently recommended decoupling the paracetamol-opioid ingredients in prescription products. The National Poison Data System (NPDS) was used to compare medical outcome of paracetamol single ingredient exposures to those associated with paracetamol-opioid combination products (hydrocodone, oxycodone, tramadol, propoxyphene or codeine combined with paracetamol). *Methods:* NPDS was searched (2000–2007) for human exposures to at least one single-ingredient paracetamol product or at least one paracetamol-opioid combination product. *Results:* A total of 468,903 paracetamol exposures were identified: 1,006 (0.2%) reported an outcome of death. Only 11% of deaths were associated with single-ingredient products

Table 1. Results by centre

CENTRE	BUCHAREST	IASI
Total number of poisonings	957	1185
AGE		
0–1 year	70 (7.31%)	117 (9.87%)
1–5 years	356 (37.19%)	381 (32.15%)
6–10 years	108 (11.28%)	129 (10.88%)
11–15 years	250 (26.12%)	309 (26.07%)
16–18 years	173 (18.07%)	249 (21.01%)
GENDER		
Male	433 (45.24%)	580 (48.94%)
Female	524 (54.75%)	605 (51.05%)
RESIDENCE		
Urban	580 (60.06%)	503 (42.44%)
Rural	377 (39.07%)	682 (57.55%)
GASTRIC LAVAGE	121 (12.64%)	250 (21.09%)
ANTIDOTES	167 (17.45%)	121 (10.12%)
SUBSTANCES	525 (54.85%)	681 (57.46%)
Ethanol	131 (13.68%)	273 (23.03%)
Caustics	55 (5.74%)	86 (7.25%)
Hydrocarbons	22 (2.29%)	75 (6.32%)
Mushrooms	15 (1.56%)	23 (1.94%)
Pesticides	40 (4.17%)	27 (2.27%)
Rodenticides	10 (1.04%)	11 (0.92%)
Toxic methemoglobinemia	15 (1.56%)	44 (3.71%)
Carbon monoxide	87 (9.09%)	24 (2.02%)
Other	143 (14.94%)	41 (3.45%)
Unknown	7 (0.73%)	77 (6.49%)
MEDICINES	386 (40.33%)	448 (37.80%)
Non-toxic	10 (1.04%)	22 (1.85%)
Bites and stings	36 (3.76%)	34 (2.86%)
COMA	146 (15.25%)	152 (12.82%)
DEATHS	2 (0.24%)-Diazinon	2 (0.17%)-methemoglobinemia -nitrites

Table 1. Number (and percentage) of deaths by exposure duration and paracetamol product type

	Acute Exposure	Acute-on-Chronic	Chronic	Unknown	TOTAL
Paracetamol single agent	62 (6)	18 (2)	15 (1)	16 (2)	111 (11)
Paracetamol-opioid	325 (32)	230 (23)	85 (8)	172 (17)	812 (81)
Both	30 (3)	16 (2)	30 (3)	7 (<1)	83 (8)
TOTAL	417 (41)	264 (26)	130 (13)	195 (19)	1006 (100)

(6% acute, 2% acute-on-chronic, 1% chronic, 2% unknown pattern). Most (81%) deaths were associated with paracetamol-opioid combination products (32% acute, 23% acute-on-chronic, 8% chronic, 17% unknown pattern). The remaining 8% of cases reported an exposure to both a combination product and a single ingredient product (3% acute, 2% acute-on-chronic, 3% chronic, <1% unknown pattern). See Table 1. *Conclusion:* The majority of paracetamol-related deaths reported to US poison centers are associated with paracetamol-opioid combination products rather than paracetamol single-ingredient products. Since the cause of death is not known for these cases (opioid-related versus paracetamol-related) the intended effect of reducing paracetamol-related injury by decoupling these products is uncertain. The root cause associated with these types of deaths is needed to address each type of exposure to develop targeted interventions.

149. Paracetamol Poisoning: Moroccan Poison Control centre Experience (1989–2007)

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Objective: Retrospective review of paracetamol poisoning received by the Moroccan poison control centre (MPCC). *Methods:* Paracetamol poisoning cases were extracted from drug poisoning cases received by telephone or by intoxication reporting form from hospitals sent to the MPCC. Demographic features, circumstances, management delay after intoxication, symptomatology, severity and outcome were analysed. The evaluation of severity was made by poisoning score severity (PSS)[1] and IPCS age groups were used. *Results:* Among 15,722 drug intoxications received during the period of study, 340 cases of paracetamol poisoning were collected (2.16%). The cases increased slightly year by year. Thus, they varied between 0 cases in 1991 to 26 cases in 1995 (3.64%). The sex ratio male/female was 0.5. The mean age was 16 ± 11.57 years (less than 1 month to 80 years). The route of exposure was oral in 92.40% and rectal in 7.6%. The most common circumstance was suicidal (50.5%); accidental exposure was noted in 48.1%. Paracetamol was used for drug abuse in 1.3%. Paracetamol was taken alone in 91.8% and associated with one or more other drugs in 8.20% of the cases. Patients presented with moderate signs (grade 2) in 25.8% or severe (grade 3) in 2.6%. The management delay after intoxication was ≤ 4 hours in 72% of the cases. Mortality was 0.5% and sequelae were observed in 3.20%, represented by liver failure. *Conclusion:* It could be shown that paracetamol poisoning has increased over the years and prevention measures are needed. *Reference:* 1. Persson HE, Sjöberg GK, Haines JA, et al. Poisoning Severity Score. Grading of Acute Poisoning. Clin Toxicol 1998; 36:205–13.

150. Epidemiology of Acute Paracetamol Poisoning: A 12-year Study in a Pediatric Poisoning Centre from Eastern Europe

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Objective: To study the evolution of epidemiology and management of acute paracetamol poisoning in a Pediatric Poisoning Centre from Eastern Europe. *Methods:* We have analyzed paracetamol poisoned patients admitted to our centre over a period of 12 years: January 1st 1997 - December 31st 2008, taking into consideration: the number of cases, age, residence, reason (accidental or intentional), poisoning severity score (PSS), serum level of paracetamol, antidote administration. *Results:* 254 patients with paracetamol poisoning were admitted during the 12 studied years i.e. 5.8% out of a total of 4632 acute poisonings with medicines. We noted a sudden increase in the number of cases in 1998, remaining at the same level in the following years. The higher number of patients: 169 (62.93%) were between 11–18 years; urban surroundings: 222 cases (87.32%) and intentional poisonings: 163 (64.39%) prevailed. Regarding the PSS we noted the following distribution: PSS3 7 cases, PSS2 3 cases, PSS1 144 cases and PSS0 95 children. Paracetamol concentration was performed in 203 patients out of the total of 254, in 158 (62%) cases being done in the first 24 hours so that the Rumack Nomogram could be used. N-acetylcysteine (NAC) was administered in 102 patients; the method of administration was: oral in 58 patients, intravenous in 44 cases and combination in 39 cases. Oral administration was prevented by adverse reactions (vomiting, abdominal pain and diarrhea) in the majority of cases (39 out of the 58) receiving oral NAC (67.24%). There were only two cases with minor adverse reactions in case of intravenous administration (2.44%). *Conclusion:* Paracetamol poisoning, considered some years before to be rare and benign, has become a real problem in pediatric toxicology in Eastern Countries. Sometimes, due to various reasons the paracetamol level cannot be used as the criteria for starting treatment with NAC. Consequently our treatment protocols should take in consideration other parameters. *References:* 1. Hendrickson RG, Bizovi KE. Acetaminophen. In: Flomenbaum NE, Goldfrank LR, Hoffman RS, et al, eds. Goldfrank's Toxicologic Emergencies. 8th ed. New York, USA: McGraw-Hill, 2006:523–37.

151. Integrated Care Pathway for the Management of the Paracetamol Poisoned Patient

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Objective: Paracetamol is one of the most common products ingested in overdose worldwide. Current UK guidelines advise assessment of risk of toxicity and, if appropriate, prompt treatment with acetylcysteine to prevent liver failure. This is difficult to achieve in busy hospital departments with targets to meet and frequent staff changes. The aim was to assess whether the introduction of an Integrated Care Pathway (ICP) would improve the management of the paracetamol poisoned patient. ICPs are multidisciplinary management plans that incorporate guidelines and best practice to enhance care and documentation. *Methods:* The specialist toxicology nurses developed, piloted and implemented an ICP for the management of paracetamol poisoning in an Emergency Department and an inpatient Toxicology Unit in 2008. Audits were carried out before and after introduction of the ICP to determine if management and documentation improved. Patients were divided according to time of presentation, 0-<4 hours, 4-<8 hours, 8-<24 hours, >24 hours, unknown time and "staggered" overdoses. Timely and appropriate blood sampling, timely treatment and accurate acetylcysteine dosage, and completeness of documentation were audited. *Results:* Data was examined for 115 patients in the pre ICP audit and 71 patients in the post ICP audit. There was a significant improvement for appropriate blood sampling (pre 94/115 versus post 69/71, p = 0.001), accurate acetylcysteine dosage (pre 25/33 versus post 45/45, p = 0.0006) and completeness of documentation (pre 67/115 versus post 66/71, p = <0.0001). Overall there was no change in obtaining timely blood sampling (pre 86/115 versus post 54/71). Variations were seen between the presentation groups with improvement to absolute compliance in 0-<4 hour but a reduction in compliance in the 4-<8 hour group. Timely

treatment was seen for all presentation groups except for 4-<8 hours. *Conclusion:* The implementation of an ICP for paracetamol poisoning improved multidisciplinary documentation and some aspects of management. Further work including refinement of the ICP and on-going education about initial triage, followed by timely blood samples and treatment is required to enhance management for patients presenting 4-<8 hours.

152. Acute Paracetamol Poisonings in the Years 2003–2008 Reported to the Toxicological Information Centre in Bratislava

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Objective: The National Toxicological Information Centre (NTIC) in Bratislava has frequently been consulted for advice on paracetamol exposures. To obtain more information about paracetamol poisonings in Slovakia, we performed a retrospective analysis of all the telephone calls to our Centre. *Methods:* All the telephone inquiries involving paracetamol exposures were extracted from our database for the years 2003–2008. The following data were analysed: age, sex, intent of exposure (accidental or suicidal), substances ingested, the clinical severity, type of first aid provided before professional medical treatment, treatment chosen. *Results:* The population under review comprised 423 intoxication cases recorded from the medical consultations provided by the NTIC over the telephone and from hospital discharge reports. Paracetamol exposures in females (64%) were more prevalent than those involving males. Intoxications in adults made up 51% of cases, with the majority of cases being suicidal intoxications. Intoxications in children up to the age of 6 accounted for 11% of cases from the population under review. These were accidental intoxications, often caused by exceeding the recommended daily therapeutic amount. Thirty-four per cent of cases were made up of intoxications of patients of the age 6 to 18 years. Suicidal cases (64%) mostly involved the combination of paracetamol with other drugs or with alcohol. Accidental intoxications (22%) were caused by paracetamol alone. Therapeutic medical treatment was carried out in these forms: ingestion of activated charcoal (55% of cases), ingestion of a laxative (25%), gastric lavage (19%), physiological saline infusion (14%), haemoperfusion (4%), forced diuresis (4%), haemodialysis (2%), and ingestion of hepatoprotective drugs (3%). N-acetylcysteine as a paracetamol antidote was given in 37% of cases. Fifty-one per cent of intoxications were accompanied by mild, transient and spontaneously resolving symptoms (PSS 1). There were no fatal cases (PSS 4). *Conclusion:* Obligatory reporting of every poisoning to the NTIC including cases of poisonings not resulting in a consultation with the NTIC came into force in October 2006. Previous to this measure we received only 30% of feedback information on poisonings about which we were consulted, which did not enable us to carry out the full analysis of the efficacy of the treatment.

153. Hepatic Injury Incidence Following Opioid with Paracetamol Exposure in Non Suicidal Patients has Risen Dramatically

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Objective: To use post marketing surveillance data from US poison centers, along with US prescription data to explore the incidence of hepatic injury from non-suicidal exposure to combinations of opioid and paracetamol products over time and with various patterns of exposure. *Methods:* The AAPCC NPDS database for 2000–2007 involving exposures to one or more opioids (hydrocodone, oxycodone, codeine, tramadol, methadone, morphine, fentanyl, hydromorphone) along with paracetamol (separately or in combination) were obtained. This dataset was limited to age > = 13 years. Suicidal cases were excluded. Exposures were characterized as to none, one, or more than one combination product, and to paracetamol in combination only or additionally. Opioid prescription data were obtained from IMSHealth. *Results:* 129,422 cases were identified. N-acetylcysteine (NAC) treatment was recommended in 8,995 cases. 2,515 patients experienced hepatic injury (AST >100 IU/L) - see Table 1. Reported cases increased 65% over the 7 year period and total prescriptions for these opioids rose 48%. However, recommendations for NAC rose 253% and injuries rose 586% (all trends $p<0.01$) Use of a single combination product with additional paracetamol was more likely to result in injury than use of one or more combination products alone ($p<0.0001$). Abuse, intentional misuse and intentional-unknown were over-represented in the injured and treated subsets. *Conclusion:* The incidence of injury related to opioid and paracetamol use has increased dramatically. Most injuries were from overuse of a single combination product alone. Self-dosing of higher doses of combination products with or without additional paracetamol for pain, and abuse of combination products are likely responsible.

Table 1. Patients and combinations

	1 Combo Only	> 1 Combo Only	No Combo & Other APAP	1 Combo & Other APAP	>1 Combo & Other APAP
Case Count	6824	734	171	1117	149
Injured	1825	184	55	405	46
Percent injured	27%	25%	32%	36%	31%

154. Confusing Clinical Response to Exceptional Paracetamol Overdose. Report of Two Cases

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Objective: To describe the clinical course in two patients who had exceptionally high serum paracetamol levels. *Case series:* 1. A 43-year-old man with a history of diabetes and some alcohol overconsumption ingested 80 g paracetamol 2–3 hours before admission to hospital. Gastric decontamination was undertaken on admission. Initial S-paracetamol was 6000 µmol/L. N-acetylcysteine was started. The patient had CNS depression and developed circulatory instability. He was given iv fluids, had a noradrenaline infusion and was put on a ventilator. Initial tests showed a metabolic acidosis with a plasma lactate >15 mmol/L. Continuous hemodialysis was started. The patient was extubated the next morning. S-paracetamol 24 hours after admission was 800 µmol/L and after another 24 hours 230 µmol/L. During day 2 there was a gradual clinical deterioration with a relapse of lactic acidosis and CNS depression. The patient gradually developed hepatic failure and finally had abdominal bleeding. Multi-organ failure ensued and the patient expired on the third day after admission. Case 2. A 30-year-old, healthy woman was admitted to hospital deeply unconscious after a serious suicide attempt, verified by a farewell letter. She had a severe lactic acidosis on admission (P-lactate 20 mmol/L). S-paracetamol was 5030 µmol/L - the sample was presumably drawn many hours after the exposure. However, on admission the liver was only mildly affected. N-acetylcysteine was given instantly. The clinical course was unstable and the patient required extensive support. Because of incipient liver failure the patient was listed for transplantation. A liver was obtained but the patient died from intractable cardiac failure during the transplantation procedure. *Conclusion:* A clinical course, including early severe lactic acidosis and CNS depression, is observed in a small number of patients with excessive paracetamol overdose and exceptional serum levels. It has been postulated that the early metabolic disturbances, observed independently of hepatic failure, are related to inhibition of mitochondrial respiration and that extreme paracetamol levels as such may cause CNS depression. These phenomena require further attention.

155. Re-evaluating the Dose of N-Acetylcysteine in Massive Paracetamol Ingestion

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Introduction: Although the current N-acetylcysteine (NAC) dose is adequate for most patients with paracetamol (APAP) overdoses, the principles upon which the dose was formulated are speculative. Recent reports suggest that standard NAC dosing may be insufficient in rare cases. We present two cases of APAP ingestion where NAC dosing was altered under this premise. *Case series:* Case 1: A 32 year-old woman ingested APAP with diphenhydramine. Initial [APAP] was 5124 umol/L, with normal LFTs. The 21 hour IV NAC protocol was started and oral NAC added at 70 mg/kg Q4h. Twelve hours later her [APAP] was 5097 umol/L. Steady state [NAC] ranged 12.5–17.5 ug/mL. The patient developed lactic acidosis, hypotension and died 66h after presentation. Perimortem her [APAP] was 3310 umol/L, diphenhydramine 3400 ng/mL, LFTs and renal function remained normal, and an INR of 1.8 was attributed to NAC. On autopsy no gross hepatic necrosis was observed and death was nonspecifically attributed to multidrug ingestion. Case 2: A 54 year-old man with normal LFTs and an initial [APAP] of 7507 umol/L at unknown time, was started on 21 hours of IV NAC. Ten hours later his [APAP] was 4190 umol/L. At 18 hours the complete IV regimen was restarted and oral NAC was added as above. On day three his [APAP] was finally <66 umol/L. LFTs peaked day 5 (AST of 3641 IU/L, ALT 7783 IU/L) then declined. Although prognostic indicators remained normal, the patient died from sepsis. On autopsy an unquantified amount of microscopic hepatic necrosis was noted. *Conclusion:* The NAC regimen is based on assumptions including APAP dose and t½, liver size, and glutathione stores. In these two cases the APAP dose and toxicokinetics significantly deviated from the assumed parameters, so the NAC dose was increased. We speculate the second patient may have developed hepatotoxicity because the maintenance NAC dose was insufficient to detoxify the NAPQI generated from an exceedingly high serum [APAP] and the increase in NAC dose was initiated too late. This contrasts with the first patient where the increase in NAC occurred very early and three days later, despite persistently elevated [APAP], no hepatotoxicity resulted.

156. Paracetamol Overdose and Vomiting

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Objective: Nausea and vomiting is commonly the only symptom of early paracetamol poisoning. It is unpleasant for the patient, time consuming for nursing staff and if uncontrolled can worsen the overall prognosis, potentially leading to problems of electrolyte balance, renal impairment and prolonged hospital stay. Early effective control of vomiting is important for both the patient and the clinician.[1] To record how commonly nausea and vomiting (N&V) occurs following paracetamol poison-

ing, as well as investigating the time period over which it develops; whether healthcare staff and patient perceptions correlate; and which pharmacological agents were effective in controlling N&V we conducted a service evaluation on patients admitted with acute paracetamol poisoning. *Methods:* All patients between the ages of 16 and 65 suffering from nausea or vomiting associated with a history and laboratory evidence of paracetamol ingestion (either as the sole agent taken or as part of a cocktail of substances ingested) were entered into the study. Patients were observed for signs of nausea and vomiting. Staff and patients completed a *pro forma* recording the severity of the N&V. *Results:* 33 consecutive patients were recorded of whom 28 had taken a single overdose of paracetamol and presented to the hospital within four hours of ingestion. The mean dose was 13 grams and four hour paracetamol concentration 107 mg/L. Fifty per cent of the patients had ingested multiple substances. Fourteen patients were observed to vomit. There was a significant correlation between paracetamol concentration at four hours and immediate vomiting (student t Test P<0.05), though only 2 patients reported having seen tablets in their vomit. The worst time for N&V was six hours. Staff perceptions of patients' N&V correlated strongly with the patients' scores (Spearman rank 0.8 P<0.001). Twelve patients received anti-emetics at a median time of 6 hours. Ten patients received cyclizine, though 4 of these required a further dose or alternative anti-emetic (ondansetron). *Conclusion:* Patients with paracetamol poisoning commonly experience N&V in a dose-related manner that appears to be worse approximately 6 hours after ingestion. *References:* 1. Scharman EJ. Use of ondansetron and other antiemetics in the management of toxic acetaminophen ingestions. Clin Toxicol 1998; 36:19–25.

157. Paracetamol Orodispersible Tablets: A Risk for Severe Poisoning in Children?

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Objective: Childhood paracetamol ingestion including the risk of hepatotoxicity remains a significant medical problem. The issue of over the counter medications leading to unintentional ingestions by young children and the importance of child-resistant closures for liquid paracetamol preparations has been studied.[1,2] At the beginning of 2002 an over-the-counter orodispersible preparation of paracetamol was licensed in our country. The aim of this study was to investigate the risk of high-dose ingestion of fast disintegrating paracetamol tablets. *Methods:* Retrospective single-centre analysis of all cases with accidental self intake of solid vs. orodispersible 500 mg paracetamol tablets in children up to 6 years between June 2003 and August 2009. Only cases with monoingestions and available information on the ingested amount (precise or maximal dose) of paracetamol were included. *Results:* 187 children with ingestion of solid 500 mg paracetamol tablets (group 1) and 16 children with ingestion of orodispersible tablets (group 2) fulfilled the inclusion criteria. The mean age was 2.3 years (median 2.0) in group 1 versus 3.0 years in group 2 (median 2.5). The mean number of ingested tablets was 2.5 (0.3–8.0; median 2.0) in group 1 versus 4.6 tablets (1.0–14.0; median 4.0) in group 2. In group 1 the mean ingested dose was 98.7 mg/kg (range 8.3–444; median 71) compared to 157.3 mg/kg (range 29.4–538; median 100) in group 2. In group 1, 23 patients (12.3%) vs. 4 patients (25%) in group 2 were admitted to hospital for N-acetylcysteine treatment because intake was >200 mg/kg. Statistical analysis showed a tendency toward ingestion of higher doses for the orodispersible tablets compared to the solid tablets. *Conclusion:* Paracetamol as orodispersible preparation may be an important risk factor for severe paracetamol poisoning in children, because they can ingest a large number of adult strength tablets in a short time due to a pleasant taste and the fast melting in the mouth. *References:* 1. Chien C, Marriot J, Ashby K, et al. Unintentional ingestion of over the counter medication in children less than 5 years old. J Paediatr Child Health 2003; 39:264–9. 2. Assargard U, Sjorberg G. The successful introduction of child resistant closures for liquid paracetamol preparations. Saf Sci 1995; 21:87–91.

158. Vaginal Burn Injury Caused by Prolonged Retention of Alkaline Batteries

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Objective: To evaluate the risk of metal absorption and toxicity in a case of prolonged intra-vaginal retention of alkaline batteries. Diagnosis may be difficult as young girls rarely admit the self insertion.[1] *Case report:* A 16-year-old girl was brought by her mother to the gynaecology clinic for lower abdominal pain, genital itching and irritation. She revealed that one month earlier her boyfriend inserted two alkaline batteries (type-AAA) into her vagina during sexual intercourse. The patient denied sexual abuse. Physical examination revealed a healthy 70 kg girl with normal vital signs, including body temperature. Laboratory data on admission showed leucocytosis (19,500 cells/mm^3) with normal haemoglobin concentration (13.5 g/dL) and mild increase of C-reactive protein (1.5 mg/dL). Pelvic examination was performed under anaesthesia because of intense inflammation and pain. Vaginal foreign bodies (two cylindrical alkaline batteries) were extracted. These were slightly eroded and not conclusively intact. The vaginal mucosa was brown, haemorrhaged easily, and difficult to evaluate owing to a copious grey vaginal discharge. Cultural exam of the vaginal discharge was negative for infections. Vesicle and rectal fistulas were excluded and vaginal irrigation performed. Antibiotics were administered in addition to vaginal healing tablets. Blood (B) and 24-hours urine (U) samples were collected in order to exclude metal toxicity. Cadmium (B = 0.4 mcg/L; U = 0.1 mcg/L), manganese (B = 0.2 mcg/L; U = 0.4 mcg/L), lithium (B = <0.1 mcg/L; U = <100 mcg/L), zinc (B = 154 mcg/dL; U = 248 mcg/dL), lead (B = <0.1 mcg/dL; U = <0.5 mcg/dL) and copper (B = 126 mcg/dL; U = 41 mcg/dL) were within normal ranges. One month after initial evaluation, healing was complete and no stenosis was evident. *Conclusion:* Prolonged retention of batteries may cause severe local burns[2] and metal toxicity. Where battery content leakage is noted metal levels should be evaluated. In this case metal toxicity did not develop despite one month of vaginal mucosal exposure to metals released by the batteries. *References:* 1. Dahiya P, Agarwal U, Sangwan K, et al. Long retained intravaginal foreign body: a case report. Arch Gynecol Obstet 2003; 268:323–4. 2. Huppert J, Griffeth S, et al. Vaginal burn injury due to alkaline batteries. J Pediatr Adolesc Gynecol 2009; 22:133–6.

159. Heavy Metals Slow Release from Retained Lead Projectiles and Thermometer's Mercury

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Objective: To report three cases in which lead (case 1, 2) and elemental mercury (case 3) were slowly released from retaining tissues without clinical/toxic effects. *Case series:* Case 1: In a shooting accident, a 67-year-old man was hit by 200 pellets in the posterior head, right shoulder and arm. He presented with severe arm oedema, so fasciotomy with subsequent antibiotic therapy was performed. He was discharged without sequelae 20 days later. During the following year he remained asymptomatic; three-monthly blood and urine lead levels, gave results 4, 14, 13, 7 mcg/dL ("normal" range 0.1–10 mcg/dL) and 19.4, 16.2, 55.6 mcg/L ("normal" range 0.5–3.5 mcg/L) respectively. Case 2: a 43-year-old man was accidentally hit by 150 pellets in the right leg during a game-shooting expedition. The patient required emergency surgery. During the following year blood lead levels (tested five times) ranged from 21.7 to 29.7 mcg/dL; urine lead levels progressively decreased from 17.8 to 2.7 mcg/L. In both cases 1 and 2 red cell zinc-protoporphyrin, urine aminolevulinic-acid and blood film results were always normal. Case 3: a 31-year old woman, visited one week after accidental inoculation of thermometer mercury, presented with local oedema and numerous radio-opaque micro-droplets localized at the second proximal phalanx of the left hand; after surgical toilette a second X-ray showed diffused foreign material over the second metacarpal joint. During a three year follow-up the patient remained asymptomatic. No biochemical alterations or modification of distribution of radio-opaque material were registered. Six-monthly blood mercury levels gave values 5.0, 1.2, 15.0, 13.0, 4.0, 1.2 and 1.9 mcg/L ("normal" range 1.0–4.5 mcg/L); corresponding urine levels were 6.5, 1.0, 9.0, 4.0, 6.0, 2.7, 4.5 mcg/L ("normal" range 0.1–4.5 mcg/L). *Conclusion:* Overall management of cases involving prolonged absorption of heavy metals due to retention of foreign bodies is not well defined. Metal absorption could be influenced by unpredictable and varying factors. Surgical removal may be difficult and incomplete. Clinical and toxicological monitoring is important for early diagnosis and possible chelation therapy. In our three cases chelation was not required, and only moderate metal releases without clinical manifestations were documented.

160. Subcutaneous Unspecific Inflammation and Granuloma Formation due to Elemental Mercury from a Broken Thermometer

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Objective: In subcutaneous tissue elementary (metallic) mercury slowly oxidizes to soluble mercuric salts that can promote local inflammation as they react with the sulfhydryl groups, resulting in enzyme inhibition and pathologic alteration of cellular membranes. Furthermore, soluble mercury salts can enter systemic circulation causing systemic toxicity. This case report presents rarely described clinical and histological changes due to subcutaneous application of elementary mercury. *Case report:* An 18-year-old man accidentally penetrated his left thenar with a broken thermometer. At the Emergency Department the broken glass was removed from the injury and the skin sewed. One week later the patient noticed local pain, skin redness and swelling 1–2 cm laterally from the injured site that progressively increased during subsequent weeks. After 6 weeks the patient was admitted to surgery outpatient due to persistent local pain, swelling, skin redness and a limited range of motion of the right thumb. On clinical examination the right thenar was painful with local reddish swelling. Radiographs revealed many spherical particles of metallic density above the metacarpal bone. An ultrasound scan revealed an area of speckled hyperechogenicity in the subcutaneous tissue just above the thumb extensors. Blood and urine mercury concentrations were slightly increased (12.3 µg/L and 14.9 µg/L, respectively). Inflamed skin was excised and the wound was irrigated with normal saline. A histological examination of the biopsy specimens revealed several small dark stained spots (mercury globules) in the dermis and subcutis, surrounded by prominent inflammatory cell infiltrate composed of eosinophilic granulocytes, neutrophils, lymphocytes, plasma cells and macrophages. Some giant cells of the foreign body reaction type around the mercury globules were also noted. The local symptoms and signs gradually subsided and the thumb regained full function within weeks. *Conclusion:* Subcutaneous elementary mercury from a broken thermometer can cause an inflammatory

response with local swelling, pain and movement deficit due to nonspecific inflammation and granuloma formation as a result of a foreign body reaction. An early and thorough excision of injured tissue containing droplets of elementary mercury is essential.

161. Lead Exposure by Accidental Ingestion

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Objective: The toxicological impact of ingested metallic lead is low, but an increased absorption of lead in children has been described.[1] *Case report:* Two children (6-year-old girl, 8-year-old boy) without symptoms were referred because they had eaten lead beads from a bag for joint-resting. The PIC Erfurt recommended an abdominal X-ray after 48 hours and further measures depending on the result. The radiography showed beads in the small and large intestine and these were still visible after 5 days in the boy. The lead blood levels increased to 275 µg/L in the boy and 230 µg/L in the girl, respectively. Both lead blood levels were above the Human Biomonitoring levels of HBM I (100 µg/L) or HBM II (150 µg/L), respectively.[2] Oral treatment with 2,3-dimercaptopropane-1-sulfonate (DMPS) was started as an in-patient for the first few days. Afterwards, the DMPS treatment was continued as an outpatient and well tolerated. However, after 17 days, the administration of DMPS was interrupted because of coxsackie virus infection in both children. At that time, the lead blood levels were already considerably decreased. Furthermore, the lead beads were no longer seen radiologically and the children remained free of symptoms of lead poisoning at all the times of monitoring. *Conclusions:* The ingestion of small lead particles by children can cause a relevant rise of the blood lead level. The passage through the bowel can be delayed and should be monitored radiologically.[3] Treatment with a chelating agent should be considered. *References:* 1. Kosnett MJ. Lead. In: Olson KR, ed. Poisoning and Drug Overdose. 5th ed. New York, USA: Lange Medical Books / McGraw-Hill, 2007:237–42. 2. Kommission "Human-Biomonitoring" des Umweltbundesamtes. Stoffmonographie Blei; Referenz- und Human-Biomonitoring-Werte (HBM). Bundesgesundheitsblatt 1996; 39:236–41. 3. Aks SE, Harris V. Radiologic Findings. In: Erickson TB, Ahrens WR, Aks SE, et al, eds. Pediatric Toxicology. 1st ed. New York, USA: McGraw-Hill, 2005:188–96.

162. Acute Nickel Toxicity: Case Report

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Objective: Acute poisonings by ingestion of divalent nickel salts are very rare, so clinical manifestations, biochemical disturbances and sequelae of severe poisoning are described. *Case report:* A 47-year-old male accidentally drank electroplating liquid containing 450 g/L of nickel sulfate and chloride salts. He promptly developed symptoms which included excitement, sweating, nausea, vomiting, abdominal pain and diarrhea. On admission 3 hours post-ingestion, the patient was alert, restless and diaphoretic. The rest of the physical examination was unremarkable except for midepigastric tenderness and hyperactive bowel sounds. BP was 200/120 mmHg, HR 105 beats/min, RR 20/min, temperature 36.8 °C. During the next 4 hours blood pressure had fallen to 80/60 mmHg despite vigorous volume replenishment, and oliguric renal failure developed. The patient's condition progressively deteriorated with coma, respiratory failure and development of bleeding. Clinical course was complicated with bilateral pneumonia. Brain CT scan did not reveal any pathological finding. The patient needed two courses of hemodialysis and mechanical ventilation for 14 days. ABG on admission showed acidosis with pH of 7.199. All biochemistry disturbances were transient, with the highest values of BUN (45.1 mmol/L), creatinine (677 µmol/L), total bilirubin (59 µmol/L), AST (268 u/L), ALT (139 u/L), CK (7031u/L), LDH (1938 u/L) and lowest value of glucose (1.7 mmol/L) within the first week post-exposure. The number of platelets reached minimum of 9 x $103/mm^3$. Nickel concentration in serum on admission was 19.02 mg/L, and in the first 24h urine was 124 mg/L. After almost two months of hospital treatment, the patient recovered from the acute phase of poisoning. However, he had symptoms of encephalopathy with altered mental state, decreased activity and motor incoordination. Neurophysiological and ophthalmological investigations revealed severe polyneuropathy with both motor and sensory involvement and partial blindness. *Conclusion:* This case is unique for several reasons. Firstly, the concentration of nickel in patient's serum, blood and urine was much higher than in previously reported cases. Secondly, this is the first description of acute oral human poisoning with divalent nickel salts with clinical picture of acute renal failure, DIC and multiorgan toxicity. Finally, the patient developed neurological sequelae as a consequence of nickel toxicity.

163. TOXBASE® in Europe

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Objective: To investigate the use of TOXBASE® (UK Internet poisons database) by European poisons centres. *Methods:* TOXBASE® accesses by European poisons centres were analysed for number of product accesses and accesses to the active ingredients within these products. A comparison was made between access to generic pharmaceutical names and trade names. *Results:* In 2005 the UK Health Protection Agency agreed to allow free access to TOXBASE® for European poisons centres. Poisons centres in 20 countries registered. Two countries already used the database: Ireland (contract to provide TOXBASE® to Irish ED users) and Iceland (since 1985). Of these 22 countries, 15 (68.2%) used TOXBASE® in the year 1 November 2008 to 31 October 2009 and 7 of these had more than 200 product accesses in the year (mean 2037, median 1054, range 212–11,276). Most common accesses were pharmaceuticals, > 55% of accesses except for Latvia who accessed only 15%. Top products accessed were: Austria (quetiapine, trazodone, hydromorphone); Belgium (paracetamol, domperidone, trazodone); Czech Republic (tea tree oil, cetirizine, sibutramine); Iceland (paracetamol, Seroquel [quetiapine], ibuprofen); Ireland (paracetamol, Nurofen for Children [ibuprofen], Lexapro [escitalopram]); Latvia (*Amanita gemmata*, cannabis, tear gases); and Poland (paracetamol, quetiapine, carbamazepine). Users of TOXBASE® may access information either via the generic pharmaceutical entry or using a trade name for that pharmaceutical. For the most commonly accessed pharmaceutical in each country a ratio was calculated of the total number of accesses to generics + trade names containing that pharmaceutical to the number of accesses to the generic entry. This gave ratios of: Austria 1.1; Belgium 1.2; Czech Republic 1.1; Iceland 1.6; Ireland 3.0; Poland 1.0). Latvia accessed very few pharmaceuticals so the calculation was not possible. The higher proportion of trade names accessed by the Irish PC is probably due to the fact that trade names specific to Ireland have been added to TOXBASE®. *Conclusion:* Some European poisons centres have made extensive use of TOXBASE®. Queries varied in different countries but paracetamol enquiries were common in 4 countries and quetiapine in 3. Apart from Ireland and Iceland most countries used the generic name rather than a trade name to access information on TOXBASE®. *Acknowledgement:* The authors appreciate the assistance of the other Units of the NPIS in supporting the database.

164. Quality Assurance and an Internet Poisons Database

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Objective: To assess end-users' experience of TOXBASE®, the UK Internet poisons information database used by medical professionals. *Methods:* TOXBASE® users were invited to complete quality assurance questionnaires during online sessions between 01/04/09–30/09/09. Users indicated how often they used TOXBASE®, why they used it, and rated on a scale of 1–6 (1 = "disagree completely" / 6 = "agree completely") a series of statements about the database. Overall responses, and those from different user groups, were compared. *Results:* 799 returns were received in total: NHSDirect/NHS24 (public access services staffed by nurse advisors) 233 (29.2%); other nurses 197 (24.6%); hospital doctors [all grades] 223 (27.9%); pharmacists 48 (6.0%), ambulance personnel 36 (4.5%), general practitioners 35 (4.4%), and "others" 27 (3.4%). The percentages of TOXBASE® accesses made by similar groups for the same time period were NHS Direct/NHS 24 (22.5%), hospital based staff (other nurses, hospital doctors and pharmacists 60.2%), ambulance personnel (1.9%) and general practitioners (1.3%). 58.8% (137) of NHSDirect/NHS24 users accessed the database "daily", contrasting with 65.7% (23) of general practitioners who reported accessing only "occasionally". 24.7% (55) hospital doctors and 45.7% (90) nurses accessed "daily". Overall 49.1% used TOXBASE® for routine enquiries, 15.1% for complex enquiries and 35.8% for triage. NHS Direct/NHS 24 nurses and ambulance personnel used TOXBASE® mainly for triage (65.5% and 63.9% respectively), whereas other groups used it mainly for routine enquiries (hospital doctors 67.7%, general practitioners 60.0%, other nurses 49.7%, pharmacists 58.3%). All user types responded similarly and positively when grading statements concerning the appearance of the database, ease of use, search facility, amount of information provided and confidence in the information. They agreed "a lot" or "completely" that the information was sufficient for managing their case (84.2% [673]), that they had confidence in the information for their query (92.5% [739]). On a scale of 1–6 (1 = poor / 6 = excellent) 86.2% (689) rated their overall satisfaction 5 or 6. *Conclusion:* Irrespective of user type respondents indicated a high degree of confidence and satisfaction with TOXBASE®. The database is used in different ways by various user groups, emphasising the need to appropriately target information in Internet poisons information systems. *Acknowledgement:* The authors appreciate the assistance of the other Units of the NPIS in supporting the database.

165. A Program to Prevent Pediatric Lye Poisoning in Liberia

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Objective: Lye (caustic soda) poisoning in children is a significant problem in Liberia. Lye, a highly alkaline corrosive substance, is used in Liberia to make household soap. It is sold in markets in a pelletized form and stored in any available and generally unlabeled container. The prepared liquid soap mixture is odorless, tasteless and looks like water. As a result, children consume it unintentionally, with the assumption that they are drinking water. The outcome of this type of exposure is as expected: severe oral and esophageal injury that lead to a severely compromised lifestyle and often, death. The objective of this project was to create public awareness of the dangers of lye exposure and to implement poison prevention interventions in Monrovia, Liberia. *Methods:* In cooperation with an international humanitarian organization, funds were provided to produce print and electronic educational materials that promoted the admonitions associated with the use of caustic soda. Public service announcements were developed for use on both radio and television to create further awareness about the dangers of exposure to lye. Billboards, which contained basic health care messages about lye poisoning, were situated strategically in Monrovia. Posters with safety messages about the prevention of caustic soda ingestion were developed and distributed to area hospitals and medical clinics. Distinctive round, fluorescent green stickers which contained the words 'Poison' and 'Caustic Soda (Lye)' were developed for distribution to families as part of an educational project to teach their children to avoid containers with

lye. *Results:* Public service announcements were aired on two radio stations, appearances were made on numerous talk shows, stories were printed in two local newspapers, three billboards were erected, 500 posters were distributed to health care facilities, and 30,000 warning stickers were distributed. *Conclusion:* With modest financial support and significant local cooperation, the program was implemented successfully.

166. Carvedilol - a Special Beta-blocking Agent?

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Objective: Carvedilol is a nonselective beta-adrenergic blocking agent with additional apha-1-blocking activity. It is assumed that the alpha-1-blocking properties aggravate the hypotension by reducing peripheral resistance.[1] *Case series:* All German-speaking PCs in Germany, Austria and Switzerland retrospectively collected carvedilol poisoning cases available up to 31.12.2007 in an online database created and financed by the German Society of Clinical Toxicology. Inclusion criteria were: dose known (± 10%), follow up information available or monitoring for at least 4 hours after ingestion, no co-ingestion. *Results:* 71 cases, of which 34 were children < 6 years, were available for analysis. Follow-up information was available in 85%, patients were monitored for 4–7 h after ingestion in 15%. 46% were treated with activated charcoal, 11% with gastric lavage or ipecac. Symptoms were hypotension (n = 14), decline in blood pressure (n = 3), bradycardia (n = 14), somnolence (n = 9), dizziness (n = 3). Rare symptoms (n = 1) were vomiting, diarrhoea, lowered blood glucose level (55 mg/dL), first degree heart block, unconsciousness. In children mild symptoms were seen after ingestion of > 6.25 mg. There were no moderate intoxications up to 25 mg (24 cases). The ingestion of 50 mg led to mild symptoms in one of four cases. After ingestion of 62.5–87.5 mg all children (n = 6) showed no symptoms. In adolescents/adults ingestion of > 50 mg < 150 mg rarely led to mild symptoms. Moderate intoxications were seen in adolescents > = 150 mg, in elderly > = 250 mg, in adults > = 500 mg, more often > = 750 mg. Lowest systolic blood pressure was 73 mmHg in adolescents and 60 mmHg in adults/elderly. Lowest heart rate was 40 beats/minute. Treatment with dopamine/other catecholamines and atropine was always successful. There were no lethal poisonings. *Conclusion:* The ingestion of carvedilol in overdose leads to symptoms which seem not to differ much from other betablocking agents. The alphablocking activity does not seem to play a major role in poisonings. The toxicity of carvedilol will be compared with propranolol in a second step in order to underline these first impressions. *References:* 1. Bouchard NC, Forde J, Hoffman RS. Carvedilol overdose with quantitative confirmation. Basic Clin Pharmacol Toxicol 2008; 103:102–3.

167. Ventricular Fibrillation in a Meprobamate Self Poisoning

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Objective: Meprobamate is frequently used to prevent psychological difficulties in alcoholic abstinence. Pharmacology and toxicology of this drug are well known: coma, miosis, sedative effects and their complications like inhalation or rhabdomyolysis. Also, cardiovascular toxicity has been studied: the vasoplegic effect can be complicated by cardiac toxicity. The mechanism of myocardial impairment is not well understood. Rhythm alterations are not described in publications about meprobamate. *Case report:* A 35-year-old man, who suffered from chronicle ethanol dependence and psychotic pathology, was found unconscious in his house. Near him were found scattered 8 g of meprobamate, baclofen and alcohol. Two hours later, the GSG score was 12, arterial blood pressure was 114/79, the electrocardiogram showed a regular, sinus tachycardia of 120 per minute, without rhythm or conduction disturbances. Toxicological analyses showed only ethyl alcohol at 1.21 g/L. Carbamate blood levels could not be measured in our center. A hepatic cholestasis was found. Our therapeutic interventions consisted of a airway protection, oxygenation, gastric catheterisation and one liter of crystalloid infusion for an hour to prevent vasoplegia. Gut decontamination was not carried out. Fifteen minutes later, the patient presented a ventricular fibrillation managed with a 300 mg intravenous bolus of amiodarone and 1200 mg/24h by continuous infusion. Endotracheal intubation and sedation with ketamine and hypnomidate were carried out. The electrocardiogram after reduction showed a ventricular bigeminism, the cardiac echography showed a low ejection fraction at 0.45. One hour later, transfer to a cardiac reference center was decided. During transfer, he presented four new ventricular fibrillation events necessitating four electric shocks. Efficiency was obtained at 200 Joules. After two days observation, the patient was out of danger and returned home five days later. *Conclusion:* No case of ventricular fibrillation after meprobamate has been described in the literature. The pharmacodynamism of cardiac toxicity is not clearly elucidated but has usually a vasoplegic expression. This case shows the risk of rhythm disturbances, and in consequence, cardiac function with or without vasoplegia should be monitored in carbamate intoxications.

168. Acute Clenbuterol Overdose in a Bodybuilder Successfully Treated with a Single Dose of Oral Propranolol

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Objective: To report a case of clenbuterol poisoning in a bodybuilder. *Case report:* A previously healthy 18-year-old male ingested 40 pills of clenbuterol (total dose = 0.8 mg) in a suicide attempt. The patient experienced tremors, vomiting, headache and chest pain 30 min later and was admitted to a local emergency unit with HR = 110 bpm, BP = 100/40 mmHg, hypokalemia (2.3 mEq/L; RV = 3.5–4.5) and ST segment depression in anterior wall leads; he was treated with fluid replacement and 50 mEq of potassium to correct the hypotension and hypokalemia, respectively. The patient was subsequently referred to the university hospital (9 h post-ingestion) with the same symptoms and similar ECG; BP = 140/40 mmHg and kalemia = 3.7 mEq/L. Serum troponin was 0.02 ng/mL (RV < 0.01), and serum and urine clenbuterol levels (LC-MS, ng/mL) were 1.43 and 84.7, respectively; no cocaine or amphetamine was detected in urine screened by immunochromatography. There was no clinical improvement in the next 9 h and an echocardiogram 18 h post-ingestion showed mild systolic dysfunction with an ejection fraction of 55%. A single oral dose of 20 mg propranolol was then given 20 h post-ingestion with significant improvement 30 min later - no chest pain, BP from 120/40 to 120/80 mmHg and PR from 115 to 86 bpm. An echocardiogram 50 h post-propranolol revealed normal left ventricular systolic function with an ejection fraction of 66%, and the patient was discharged. *Conclusion:* Clenbuterol is a potent, long-acting beta2-agonist (t½ = 25–39 h). Although in Brazil clenbuterol is only authorized for veterinary use, this drug has been used illegally by bodybuilders because of its sympathomimetic, lipolytic and anabolic effects. In addition to the clinical manifestations of beta-adrenergic intoxication (hypotension, hyperglycemia and hypokalemia), clenbuterol overdose may also cause myocardial injury, as shown here, with alterations in the ECG and echocardiogram and an increase in troponin levels. As elsewhere reported, this case also suggests that the use of beta-adrenergic antagonists may be safe and efficacious in such overdoses since a single dose of oral propranolol administered 20 h after clenbuterol ingestion caused rapid improvement in all cardiovascular parameters.

169. Severe Metabolic Alkalosis in Chronic Salicylate Poisoning

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Objective: Acute salicylate poisoning gives rise to a primary respiratory alkalosis and, later in the course of severe cases, a primary metabolic acidosis. In chronic salicylate poisoning, however, no specific acid-base disturbance is typical.[1,2] We report three cases of chronic salicylate poisoning who presented with pronounced hypokalemia and metabolic alkalosis of unknown cause. *Case series:* 1. A 38-year-old female was admitted because of weakness and fatigue. Arterial blood gases revealed metabolic alkalosis (pH 7.52, PCO_2 8.6 kPa, BE +24 mmol/L). S-potassium was 2.0 mmol/L and S-standard bicarbonate 49.6 mmol/L. The patient was given saline and potassium chloride iv, which almost normalised the laboratory values within three days. Investigations concerning endocrinologic disturbances were negative and the patient denied having vomited repeatedly. Later it became clear that she had overdosed on salicylates for several months, at least 10 g/day. 2. A 63-year-old female presented disorientated and confused with a history of chronic pain. Laboratory tests showed S-potassium 1.8 mmol/L, S-salicylate 0.1 mmol/L, and a pronounced metabolic alkalosis of pH 7.73, PCO_2 5.8 kPa, BE +29 mmol/L. After two days of treatment with saline and potassium chloride iv, her condition improved dramatically. The patient denied repeated vomiting, but admitted daily overdoses of salicylate during the past years except for the last few days. 3. A 54-year-old female was admitted with impaired level of consciousness after an overdose of 50 mg diazepam and 10 g salicylates. Laboratory investigations showed S-potassium 2.4 mmol/L, S-standard bicarbonate 41 mmol/L and S-salicylate 3.4 mmol/L. Arterial blood gases displayed pH 7.55, PCO_2 6.6 kPa, BE +18 mmol/L. After treatment with repeated doses of charcoal, and saline with potassium chloride iv, her condition improved. The patient later admitted a grave daily misuse of salicylates and benzodiazepines to reduce her anxiety. *Conclusion:* Acute and particularly chronic salicylate poisoning gives rise to a pronounced hypokalemia.[2,3] We propose that in severe chronic cases, the depletion of potassium may lead to a pronounced metabolic alkalosis. *References:* 1. Bailey RB, Jones SR. Chronic salicylate intoxication. A common cause of morbidity in the elderly. J Am Geriatr Soc 1989; 37:556–61. 2. Flomenbaum NE. Salicylates. In: Goldfrank LR, Flomenbaum NE, Howland MA, et al, eds. Goldfrank's Toxicologic Emergencies, 8th ed. New York, USA: McGraw-Hill, 2006:550–64. 3. Burke A, Smyth EM, Fitzgerald GA. Analgesic-Antipyretic and Antiinflammatory Agents; Pharmacotherapy of Gout. In: Brunton LL, Layzo JS, Parker KL, eds. Goodman & Gilman's The pharmacological basis of therapeutics, 11th ed. New York, USA: McGraw-Hill, 2006:687–92.

170. Blindness Induced by Quinine: Case Report and Review of Current Treatments

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Objective: Assessment of current treatments for blindness induced by quinine. *Case report:* A 33 year old female was referred for blindness after two days of treatment with Quinimax® for falciparium malaria. She received 6.528 g of quinine and quinine serum concentration reached 14.4 µg/ml. Retinal angiography revealed neither vasospasm nor occlusion of retinal vessels. Emergency treatment advised by the poison control center included nimodipine infusion and two hyperbaric oxygen (HBOT) sessions of 90 minutes at 2.4 ATM during the

first 6 hours following the onset of blindness. A small improvement of visual acuity occurred following the first HBOT session and full recovery was obtained after the second session. This clinical improvement was contemporaneous with the decrease of serum quinine concentration. *Conclusion:* Blindness induced by quinine is a symptom of "cinchonism". It appears for doses of at least 4 grams and within the 4th to 14th hour following the overdose. The visual loss is usually associated with serum concentration above 10 µg/mL.[1] The pathophysiology remains controversial[2]: retinal ischemia by arterial vasoconstriction, direct retinal toxicity, toxic mechanism linked to cholinergic neurotransmission. Treatments to increase the elimination of quinine have not demonstrated any efficiency. Vasodilators administered orally, intravenously or retrobulbar, stellate ganglion blockage (SGB)[3,4] have been proposed. SGB is the most controversial therapy because of its potential complications and ineffective reports.[2] Lastly retrobulbar injection of vasodilator therapy is rarely reported in the literature. *Conclusion:* Consequently, HBOT appears to be a promising treatment,[5] with its known low rate of side effects. 1. Townend RS, Sturm JW, Whyte S. Quinine associated blindness. Aust Fam Physician. 2004; 33:627–8. 2. Bacon P, Spalton DJ, Smith SE. Blindness from quinine toxicity. Br J Ophthalmol. 1988 March; 72:219–224. 3. Barrett NA, Solano T. Quinine ocular toxicity: treatment of blindness using therapy for vasospasm. Anaesth Intensive Care. 2002; 30:234–5. 4. Dyson EH, Proudfoot AT, Prescott LF, Heyworth R. Death and blindness due to overdose of quinine. Br Med J (Clin Res Ed). 1985; 291:31–33. 5. Wolff RS, Wirtschafter D, Adkinson C. Ocular quinine toxicity treated with hyperbaric oxygen. Undersea Hyperb Med. 1997; 24:131–4.

171. Fatal Poisoning Caused by Felodipine

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Objective: Felodipine is a calcium-channel blocker of the dihydropyridine type similar to nifedipine. This is the first report of a fatality after ingestion of an overdose. *Case report:* A 33-year-old woman ingested 600 mg felodipine at an indefinite time before admission. She was transferred into ICU with severe vasoplegic shock with normal left ventricular function. Systemic vascular resistance was decreased to 300 dyn.sec.cm^{-5} (normal 1000 to 1500), although catecholamines were administered in maximum dose. Calcium gluconate, glucagon, insulin-glucose, and lipid emulsion were ineffective. Albumin dialysis with Molecular Adsorbents Recirculation System (MARS®) was used to remove protein bound felodipine. The catecholamine supply could be reduced temporarily, but peripheral oxygen utilisation was massively disturbed. Lactic acidosis and acute renal failure were treated with continuous venovenous hemofiltration. Despite all these measures, the critical state of the patient could not be stabilized. An abdominal compartment syndrome developed 24 hours after ingestion. A serious compression of mesenteric aortic branches with underperfusion of intestine was recognized by CT angiography. Laparoscopy showed a large increase of intra-abdominal pressure and gangrenous changes of the whole small intestine. The patient died on the following day. *Conclusion:* Massive overdose of felodipine caused exclusively a long-lasting peripheral vasodilatation resistant to all appropriate therapeutic measures. This vasoplegic syndrome corresponds to the felodipine half-life (11 to 16 hours after single dose; 22 to 27 hours after repeated doses). No cardiotoxic effects occurred in our case and has been previously reported,[1] confirming the highly selective binding of felodipine to voltage-dependent calcium channels of vascular smooth muscle cell membranes in life-threatening poisoning. The possibility of opening calcium channels by use of 4-aminopyridine (4-AP) infusion was not available.[1] *References:* 1. Magdalan J, Kochman K, Smolarek M, et al. Severe felodipine and theophylline poisoning successfully treated by 4-aminopyridine: a case report. Przegl Lek 2003; 60:268–70.

172. Fetal Effects of Diazepam Overdose During Pregnancy

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Objective: A recent study of diazepam overdose in pregnant women showed no increased risk of congenital malformations in the offspring.[1] A case report[2] and case series[3] have however detailed infants born with malformations including facial and oral clefts. The UK Teratology Information Service (UKTIS) is actively collecting data on the fetotoxic effects of diazepam overdose during pregnancy. *Methods:* Using standardised procedures, pregnancy outcome data have been collected prospectively from women who took intentional diazepam overdoses in pregnancy between 1988 and 2005. Overdose was defined as acute ingestion of more than 30 mg, the maximum daily therapeutic amount. *Results:* During the period of study, 49 pregnant women took diazepam in overdose; 35 in combination with other drugs. The doses of diazepam ingested ranged from 36 mg up to 20,000 mg. Twenty eight (57%) overdoses were taken in the first trimester, 17 (35%) in the second trimester and four (37%) in the third. Thirty six infants were liveborn, seven were spontaneously aborted and six were electively terminated. In the liveborn infants no congenital malformations were reported, although one infant was noted to have a heart murmur. The frequency of malformations in liveborn infants, if the heart murmur was indicative of an anomaly (1/36, 2.78%, 95% CI 0.15–16.21), was not significantly higher than the incidence of major congenital abnormalities in the general population. *Conclusion:* Although it is possible that the heart murmur detected was indicative of an underlying structural congenital cardiac defect, concomitant alcohol use, a well recognised cardiac teratogen, would suggest that causality cannot be attributed to diazepam. These preliminary data are reassuring, but the very small sample size means that a risk cannot be definitively excluded. *References:* 1. Gidai J, Acs N, Banhidy F, et al. No association found between use of very large doses of diazepam by 112 pregnant women for a suicide attempt and congenital abnormalities in their offspring. Toxicol Ind Health 2008; 24:29–39. 2. Rivas F, Hernandez A, Cantu JM. Acentric craniofacial cleft in a newborn female prenatally exposed to a high dose of diazepam. Teratology 1984; 30:179–80. 3. Laegried L, Olegard R, Walstrom J, et al. Teratogenic effects of benzodiazepine use during pregnancy. J Pediatr 1989; 114:126–31.

173. Myocardial Infarction Associated with Overdose of Paroxetine and Citalopram and Features of Serotonin Syndrome

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Objective: Paroxetine and citalopram are serotonin reuptake inhibitors. While paroxetine overdoses tend to be mild, citalopram overdoses have been associated with seizures and cardiac effects including tachycardia, bradycardia, QTc and QRS prolongation. Myocardial infarction has not been reported with overdoses of these agents. Serotonin syndrome can potentially occur with overdoses and drug interactions between these agents and has rarely been associated with myocardial infarction. A case of myocardial infarction associated with an overdose with paroxetine and citalopram and features of serotonin syndrome is reported. *Case report:* A 45 year old man with a history of depression and suicide attempts by overdose was found unresponsive, with muscle rigidity, foaming at the mouth, with empty bottles of recently prescribed paroxetine and citalopram. Upon arrival, paramedics gave naloxone without response and performed endotracheal intubation. At the emergency department, systolic blood pressure was 250 mm Hg. Electrocardiogram was abnormal with 1 mm ST segment elevation in leads I and aVL and ST segment depressions in II, III, and aVF. He was transferred to a tertiary care hospital's intensive care unit where he withdrew to painful stimuli, had muscle rigidity, pupils midrange and reactive, and labile vital signs. Temperature ranged from 37 to 39.4 C. Systolic blood pressure ranged from 68 to 178 mm Hg. Troponin I peaked at 15.71 ng/mL. CK-MB peaked at 6.9 ng/dU. Echocardiogram demonstrated an anterior wall motion abnormality with LV ejection fraction of 40–45%. Cardiac catheterization showed no angiographically significant coronary artery disease, though septal Q waves developed on the electrocardiogram. Hospital course was complicated by bradycardia and hypotension requiring intra-aortic balloon pump and pressor support. The patient remained unresponsive. CT scan demonstrated anoxic encephalopathy and the patient expired. *Conclusion:* Serotonin syndrome is a clinical diagnosis with exposure to serotonin agents, autonomic dysfunction, acute encephalopathy, and muscle rigidity. The case presented here was a mixed picture, with features of serotonin syndrome and citalopram overdose. He had a myocardial infarction with no angiographically significant coronary artery disease. There are prior case reports of myocardial infarction occurring in the setting of serotonin syndrome but associated with neither citalopram nor paroxetine overdose.

174. Toxicokinetics of Diltiazem and Three Metabolites During Acute Life-Threatening Poisoning

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Objective: The calcium channel blocker diltiazem is metabolized to N-demethyl-diltiazem (MA) and deacetyl-diltiazem (M1). These two active metabolites are metabolised to N-demethyl-deacetyl-diltiazem (M2) and other metabolites. Toxicokinetic data over 5 days in a near fatal diltiazem poisoning is presented. *Case report:* A 60-year-old man ingested alcohol and about 20 g diltiazem slow release formulation (Cardizem Retard). He was comatose, hypoxic, bradycardic (40/min) with AV-block and hypotensive (75/45 mmHg). He was intubated, given a temporary pacemaker and treated with calcium, insulin/glucose and massive vasopressor support. After 12 days he was stable on ventilator and transferred to his local hospital for further treatment. S-ethanol on admission was 1.4 g/L; other substances than diltiazem and its metabolites were not detected. The serum concentration of diltiazem remained high for the first 5 days after intake and then decreased slowly (Table 1). Furthermore, the concentrations of MA and M1 were relatively high and while the MA level decreased after 3 days the M1 level remained high. *Methods:* Diltiazem and its metabolites were measured in serum by a validated HPLC method with UV-detection and a coefficient of variation below 5%. *Conclusion:* The prolonged clinical course with sustained elevated level of diltiazem in this patient could be due to diltiazem inhibition of its own CYP3A4-mediated metabolism. Diltiazem is a mechanism-based inhibitor of CYP3A4 *in vitro* and a 62% decrease in small bowel CYP3A activity has been demonstrated in patients receiving therapeutic doses of diltiazem.

Table 1. Diltiazem and metabolites

Day	Diltiazem (ng/mL)	MA (ng/mL)	M1 (ng/mL)	M2 (ng/mL)
1	3436.8	1524.6	1019.1	32.4
2	3313.5	1177.6	979.1	137.4
3	2450.4	1066.2	672.8	72.9
4	3159.5	320.3	1374.9	156.8
5	3815.0	115.5	1209.9	15.2
6	2367.9	79.9	645.6	0.0

175. Clinical Toxicometry of Acute Poisonings by Fenazepam in Older Children

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Objective: In recent years the most frequent causes of poisoning in children were tranquilizers - derivatives of benzodiazepine, mainly fenazepam, and in 2008 this reached 15.9% of patients admitted to Moscow Pediatric Toxicological Center compared to 9.7% in 2001. The highest incidence of up to 46% was registered in children of older school age. The aim of study was the determination of concentration thresholds wherein basic symptoms of fenazepam poisoning were demonstrated. *Methods:* Determining of fenazepam blood concentration in children aged 11–14 years and comparison of the obtained results with clinical symptoms of poisoning. *Results:* Fenazepam [7-bromo-5-(2-chlorophenyl)- 1,3-dihydro- 2*H*- 1,4-benzodiazepin-2-one] has been used in clinical practice since 1978 to check attacks of irritancy, emotional stress and lability, anxiety, reactive psychosis and cenesthopathic hypochondriacal disorders. It is manufactured in pills and ampoules. One of the basic symptoms of poisoning by fenazepam is depression of consciousness from somnolence to coma, psychomotor excitement accompanied by visual or acoustic hallucinations in some patients. Muscle hypotension and ataxia, and also dysarthria and decreased tendon reflex appear at an early stage. The changes in cardiovascular system can manifest themselves as tachycardia or bradycardia, dropping of arterial tension. ECG demonstrated rhythm disturbances such as sinus tachycardia or bradycardia. Fenazepam blood concentrations were determined by HPLC in 20 children aged 11–14, admitted to Moscow Pediatric Toxicological Center. The fenazepam blood levels and main symptoms of intoxication registered are presented below. At the level 2.50 ± 1.55 ng/mL there was somnolence, pupils of medium dimension, skin of usual colouring; from 2.65 ± 0.95 ng/mL initial ataxia; from 2.76 ± 0.98 ng/mL tachycardia, muscle hypotension; at concentration 3.25 ± 0.55 ng/mL - soporific condition developed, 4.02 ± 0.3 ng/mL caused initial coma. *Conclusion:* Thus, a fenazepam concentration of 2.50 ng/mL was evaluated as the threshold, characterizing slight poisoning, from 3.25 ± 0.55ng/mL as medium severity, and from 4.02 ± 0.3 ng/mL as severe.

176. Intentional Warfarin Overdose and Coagulopathy: Two Case Reports

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Objective: Deliberate warfarin overdose is uncommon. The onset and duration of coagulopathy are variable making it difficult to establish an appropriate period of observation.[1,2] This report describes two cases that presented to hospital soon after deliberate overdose and in whom coagulation status was closely evaluated. *Case series:* Case 1 was a 20-year-old woman who presented 5 hours after deliberate ingestion of warfarin 285 mg and aspirin 150 mg. She had been prescribed warfarin after lower limb thrombosis but had not complied with therapy in the preceding 3–4 weeks. Case 2 was a 53-year-old man who presented three hours after deliberate ingestion of warfarin 56 mg. He had been receiving warfarin due to a pulmonary embolism four years earlier, and INR was 2.1 five days before presentation. Baseline electrolytes and liver biochemistry were normal in both patients. Prothrombin time was studied with respect to the interval after warfarin ingestion. Prothrombin time progressively increased for more than 48 hours after ingestion, as reported elsewhere (2). Intravenous vitamin K was administered, 1 mg at 72 hours post-ingestion in case 1, and 0.5 mg at 60 hours post-ingestion in case 2 (Table 1). No haemorrhagic complications occurred. *Conclusion:* Maximal coagulopathy may not occur until several days after warfarin overdose, and patients should be monitored for long enough to allow this to be detected. *References:* 1. Isbister GK, Hackett LP, Whyte IM. Intentional warfarin overdose. Ther Drug Monit 2003; 25:715–22. 2. Ramanan AV, Gissen P, Bose-Haider B. Intentional overdose of warfarin in an adolescent: need for follow up. Emerg Med J 2002; 19:90.

Table 1. Prothrombin time (PT) and international normalised ratio (INR) after warfarin overdose

Case 1: Interval (h)	PT	INR	Case 2: Interval (h)	PT	INR
5.3	12	1.0	3.4	26	2.2
13.6	13	1.1	6.6	28	2.4
20.5	16	1.4	14.4	35	3.0
24.9	20	1.7	21.9	55	4.6
31.1	26	2.1	33.3	59	5.0
37.4	32	2.6	39.9	81	6.7
44.4	45	3.6	47.0	81	6.7
53.7	58	4.6	55.1	85	7.0
61.5	74	5.8	62.7*	58	4.8
67.2	84	6.6	85.0*	51	4.3
76.5*	21	1.7			
88.9*	19	1.6			

*after administration of intravenous vitamin K

177. Pregabalin Overdose in Adults and Adolescents - Experience in Sweden

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Objective: Pregabalin was introduced on the Swedish market at the beginning of 2005 for treatment of epilepsy. Today the indications also include generalized anxiety syndrome and neurogenic pain. The prescription rate of pregabalin has increased dramatically in Sweden, and an increasing number of inquiries related to overdose has been observed. So far only a few case reports after overdose with pregabalin have been reported in the literature. In order to assess the acute toxicity of pregabalin, a retrospective survey of hospital case records received by the Swedish Poison Information Centre was carried out. *Case series:* Since the introduction of pregabalin the Poisons Centre has received 485 calls concerning overdose in adults and adolescents. Many of these dealt with mixed poisoning. During the actual period 42 cases of pure pregabalin poisoning could be analysed in detail by studying hospital case records. The patients in this material were 15 to 61 years old, 69% were females and 31% males. The ingested dose ranged from 750 mg to 30 g (mean 5.3 g, median 4.2 g). The reasons for overdosing were self destructive behaviour/suicidal attempt (86%) and abuse (14%). The severity of poisoning was graded according to the Poisoning Severity Score (PSS). Twenty-one patients (69%) developed mild symptoms (PSS 1), 11 patients (26%) developed moderate symptoms (PSS 2) and one patient developed severe symptoms related to aspiration (PSS 3). The most frequent symptoms were mild CNS depression (20/42), tachycardia (10/42), tremor/muscular twitching (7/42), seizures (5/42) and unconsciousness (4/42). Seizures were seen occasionally in doses above 3.7 g. Other symptoms seen in a few cases were dizziness, agitation, facial myoclonus, nystagmus and urinary retention. Occasionally headache, disorientation, blurred vision, incoordination and mild hypotension occurred. At doses below 3 g most patients had mild symptoms. *Conclusion:* In this series most cases of pregabalin overdose were benign. The most severe symptoms were seizures and CNS-depression. In general, doses below 3 g produced minor symptoms. Some patients had taken large doses without developing serious symptoms. This is possible due to inter-individual variations in sensitivity or development of tolerance, making it difficult to establish a precise dose-response relation.

178. Ischemic Colitis Following Duloxetine and Lamotrigine Poisoning: Is There a Relationship?

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Objective: We report a case of duloxetine and lamotrigine poisoning complicated by ischemic bowel necrosis. *Case report:* A 66-year-old woman was brought comatose (GCS 3) to the emergency department 12 hours after ingestion of lamotrigine 2100 mg and duloxetine 1440 mg. Because of severe hypoxemia and aspiration pneumonia, the patient was intubated; hypotension required infusion of dopamine and norepinephrine. At admission to the ICU an extensive gastric lavage was performed, initially followed by oral administration of multiple-dose activated charcoal and cathartics, and subsequently by polyethylene glycol (PEG) whole bowel irrigation. Duloxetine and lamotrigine blood levels were 730 ng/mL and 16 micrograms/mL, respectively. On day 2, some liquid stools interspersed with charcoal were produced, but intestinal hypoperistalsis persisted. Neostigmine 0.2 mg as well as colonic enema were administered without any improvement; therefore PEG administration was continued for the next 5 days. Coma was prolonged for eight days but there were no abnormalities on magnetic resonance imaging; on day 9 the patient progressively recovered consciousness and was extubated on day 10. On day 15 the patient complained of vomiting and severe abdominal pain. Gastric endoscopy revealed the presence of charcoal entrapped in the stomach; abdominal X-ray showed dilatation of both small bowel and colon; at laparotomy the caecum and terminal ileum were found to be necrotic. Ileocolic resection was performed: about 5 kg of faeces were evacuated. Her subsequent recovery was uneventful and she was discharged 15 days later. *Conclusion:* Ischemic colitis (IC) in acute poisoning is a rare event, mainly described in severe patients admitted in ICU.[1] There is no evidence directly linking either duloxetine or lamotrigine with IC. In our case, vasopressors-related IC was ruled out because of lack of temporal relationship but many other causes may have contributed: hypotension and multiorgan hypoperfusion could explain the pathogenesis of an hypoxic injury; moreover, duloxetine-induced constipation (a well known side effect during therapy) and impacted faeces which had progressively pressed against the bowel wall may have substantially contributed to bowel ischemia. *References:* 1. Nault JC, Mégarbane B, Théodore J, et al. Poisoning-related bowel infarction: characteristics and outcomes. Clin Toxicol 2009; 47:412–8.

179. Bupropion Overdoses Presenting to US Emergency Departments

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Introduction: Bupropion is an atypical antidepressant commonly used for depression and smoking cessation. It is structurally dissimilar to other antidepressants and is an inhibitor of norepinephrine and dopamine uptake. It is well known to cause seizures in overdose. The published data regarding bupropion toxicity involves mostly case reports and a large case series summarizing US poison center data. Limited systematic data of consecutive emergency department (ED) overdoses are available. *Objective:* To assess the incidence of seizure in cases of bupropion toxicity presenting to emergency departments. *Methods:* Design: A multi-center retrospective ED study design was utilized. Subjects: Consecutive patients with the primary ED diagnosis of antidepressant overdose were identified from January 1, 2008 to September 30, 2009. Epidemiologic data was collected as well as the occurrence of seizure,

arrhythmias, serotonin syndrome or need for endotracheal intubation. *Results:* Out of 1,590,248 consecutive ED patients from 20 EDs, 355 patients were identified with the primary final diagnosis of antidepressant overdose. Of these, 33 cases involved bupropion as the primary toxicant. The mean age of study subjects was 27.2 years (range: 1.5–58.7 years), 30% were male, 67% of cases were intentional ingestions with the mean bupropion dose ingested, by history, of 1267 mg (range: 50–4500 mg). Seizures occurred in 5 of 33 cases (15%) with only one case having more than one seizure. There were no cases of status epilepticus. No cases were associated with arrhythmias, serotonin syndrome, or the need for endotracheal intubation. *Conclusion:* Bupropion overdose is rarely associated with seizures. Severe complications from overdose are uncommon in cases presenting to US emergency departments.

180. Venlafaxine Emergency Department Overdoses are not Associated with Significant Morbidity and Mortality

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Introduction: Venlafaxine is an antidepressant that effects several neurotransmitters including serotonin, norepinephrine, and dopamine. Several cases have been reported documenting severe outcome from overdose. Few studies are available regarding overdose involving this toxicant. *Objective:* To assess the incidence of toxic effects in cases of venlafaxine overdoses presenting to emergency departments. *Methods:* Design: A multi-center retrospective Emergency Department (ED) study design was utilized. Subjects: Consecutive patients with the primary ED diagnosis of antidepressant overdose were identified from January 1, 2008 to September 30, 2009. Cases that involved venlafaxine as the primary intoxicant and intentional overdoses were identified. Epidemiologic data was collected as well as the occurrence of seizure, arrhythmias, serotonin syndrome, or need for endotracheal intubation. *Results:* Out of 1,590,248 consecutive ED patients from 20 EDs, 15 patients were identified with venlafaxine overdose. All cases were intentional and involved venlafaxine as the primary toxicant. The mean age of study subjects was 37.6 years (range: 16–65 yrs), 75% were female with the mean dose ingested by history of 2562 mg (range: 750–4500 mg). Six of 15 patients were tachycardic (40%). The mean heart rate was 102 (range: 74–157 bpm). There was poor correlation between the heart rate and dose ingested ($r = 0.41$). Seizures occurred in 1 of 15 cases (7%) with no cases of status epilepticus. One patient required endotracheal intubation (7%) and no cases were associated with arrhythmias, serotonin syndrome or death. *Conclusion:* Venlafaxine overdose is uncommon and rarely associated with significant morbidity and mortality in intentional ingestions presenting to US emergency departments.

181. Injuries in the Maritime Sector Reported to the Spanish Poison Control Centre (2005–2009)

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Objective: Epidemiological studies concerning exposure to chemicals carried or used aboard or among shipyard workers are scarce. Many of these events occur in outbreaks in confined spaces. The Spanish fleet is one of the biggest in the world and consists mainly of fishing ships, but also oil and chemical tankers, container ships and ferries. The goal of this work is to evaluate the intoxications occurring in the maritime sector of Spain. *Methods:* Retrospective analysis of intoxications on board and in shipyards received by the Spanish Poison Control Centre from April 2005 to October 2009. Data included gender, age, type of product, route of exposure, clinical features, and site of exposure. *Results:* A total of 69 cases were reported, 75% were male and 81% adults. Routes of exposure were as follows: respiratory 33.3%, ocular 32.8%, oral 23.2%, and others or mixed exposures (10.7%). Industrial products were responsible for 51%. The most common products implicated were: paints and solvents including xylene, benzene and styrene (17 cases), cleaning products (12), resins (6), freon (3), methane (1), and mixtures (7). Therapeutic drugs were involved in 6 occasions. Four episodes involved several individuals (asbestos, ciguatera, gas oil, and hydrogen sulfide plus carbon monoxide). Health care facilities called in 94.2% of cases, 26.3% from the Radio-Medical Centre. Poisonings took place on board on 51 occasions, 3 of them among passengers of a ferry, 2 in the ship's hold, 1 in a container, 1 in a cabin. Ten cases occurred far from the coast. Seven episodes occurred in the shipyard. At the moment of the consult, 42 patients were symptomatic. Common manifestations were ocular (33.3%), dermal (30.9%), and neurological (26.2%). Estimated outcome was: mild 10 patients, moderate 28, severe 8. One patient died after the inhalation of hydrogen sulfide and carbon monoxide. Only 2 cases were suicidal, the rest accidental: occupational (41), unintentional general (16), therapeutical errors and others (10). *Conclusion:* This study shows that the majority of injuries involved industrial products. Poison Control Centres should be prepared for the possibility of moderate or severe injuries affecting several individuals with a lack of access to qualified medical assistance.

182. Enquiries to the Danish poison Information Centre (Giftlinjen) About Drug Overdosing in relation to Suicide Attempts or Affective Reactions

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Background: A substantial number of enquiries to the Danish Poison Information Centre (Giftlinjen) are related to the toxic effects of drugs after overdosing due to suicidal attempts or affective reactions. It is important to identify specific patient or drug groups involved to set up procedures in order to reduce the number of these patients. *Objective:* A descriptive study in which all enquiries to Giftlinjen in the period 01/05/07 - 30/04/08 (1 year) concerning suicidal attempts or affective reactions were reviewed. *Results:* In the period there was in total 1461 enquiries (1026 women, 431 men) with the category "suicide attempt or affective reaction" as the reason for contacting Giftlinjen. Of those, 1277 were related to drug overdosing. A major part of the enquiries came from emergency rooms or hospital departments (82%) and were categorised as "requiring treatment" or "life-threatening" in 56% and 21% of the cases, respectively. In 629 cases (72%) the patients ingested a single drug and the 5 most frequent were ibuprofen (80 cases), paracetamol (65 cases), chlorprothixene (57 cases), citalopram (35 cases) and zopiclone (24 cases). In 228 cases (16%), the patients ingested more than 1 drug - either in therapeutic doses or in toxic doses (defined as any ingestion above the therapeutic dose). The 5 most frequent were paracetamol (99 cases), ibuprofen (68 cases), zopiclone (60 cases), citalopram and escitalopram (42+14 cases) and chlorprothixene (30 cases). In 30 of the 99 multiple drug overdosing cases with paracetamol, the patients ingested an overdose of another drug (16 together with ibuprofen, 2 with zopiclone, 4, with chlorprothixene, 3 with citalopram and 2 with escitalopram). *Conclusion:* The majority of the patients are women taking an overdose (single drug) of an easily available analgesic drug. However, a substantial number of patients take more than one drug - often psychoactive drugs - which could lead to a more serious poisoning. The treating physician has therefore to be especially aware of drug-drug interactions in these patients who may be poisoned with more than one drug at the same time.

183. Oslo 2008: A One Year Prospective Study of 1357 Poisoned Adults Hospitalized in Oslo

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Objective: In a one year prospective multicenter cohort study of all poisoned patients seeking medical attention in Oslo (total inhabitants 578,870), data from the group admitted to hospital is presented here. The aims were to study type of poisoning, treatment, complications and psychiatric and demographic characteristics and compare data with a similar study from 2003. *Methods:* Patients aged ≥ 16 years in Oslo admitted to hospital with the diagnosis of acute poisoning. A standardized interview was completed by the physician on duty, documenting clinical parameters and socioeconomic and psychiatric aspects. *Results:* There were 1357 hospitalizations from acute poisonings during the period, 29% more than in 2003. Fifteen patients died (1.1%) during hospital stay and 19 survived with sequelae (1.4%), mainly anoxic brain damage. Forty-seven per cent were men and 53% women. Median age was 35. The most frequently taken main agent was ethanol (17%), followed by benzodiazepines (14%), paracetamol (11%), GHB (8%), benzodiazepine derivates (7%), and opiates (6%). Twenty per cent presented with coma (GCS<8). The most frequent complications were respiratory insufficiency (11%), prolonged QTc (6%) (mainly associated with SSRI or "party dope" poisonings), pneumonia (3%), arrhythmia (3%), hypothermia (3%) and seizures (3%). The interviewing doctors defined 14% of the poisonings as a definite suicidal attempt, 36% as a possible suicide attempt and 34% as accidental drug overdoses. *Conclusion:* Acute poisoning is an increasing cause for admission to hospitals in Oslo. Ethanol and benzodiazepines are still the most frequent main toxic agents. GHB poisonings are increasing and have now passed the incidence of hospitalized opioid poisonings. Paracetamol poisonings have not increased although the distribution has expanded. Interestingly, there has been an increase in poisonings believed to have a suicidal intention.

184. Carbon Monoxide Poisoning by Indoor Barbecue Reported to Different German Speaking Poison Information Centers and the BfR Berlin

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Objective: From 2008 up to now the Poison Information Center (PIC) Erfurt has registered 4 incidents involving: 3, 4, 2 and 3 (1 fatality) persons with signs of carbon monoxide (CO) poisoning from indoor barbecues (COBIB). To explore if COBIB is a new phenomenon in Germany, although one which was already described in other countries,[1] we asked 10 German-speaking PICs and the BfR Berlin to send us all their COBIBs from the last ten years. *Methods:* A retrospective study of all COBIBs reported to the German-speaking PICs and the BfR Berlin from 2000 to the end of August 2009 was performed. *Results:* 57 COBIBs (accidental: 94.2%, suicidal: 3.8%, unknown reason: 2.0%) with 143 persons involved were reported by 5 of 11 German-speaking PICs and the BfR Berlin. The other 6 PICs either did not register any COBIBs or could not separate them in their database from other CO poisonings. The number of COBIBs and involved per-

sons increased from one incident with 2 persons in 2000 to 17 incidents with 32 persons in 2009 (to the end of August), respectively. The 143 persons with COBIB (female and male 26.6% each, unknown gender 46.8%) were distributed over 15 of 16 federal states of Germany and Switzerland with centers in Bavaria (22), Brandenburg (18), and Baden-Wuerttemberg (16). The age distribution was: adults (57.3%), children (25.2%), and unknown (17.5%). The severity of initial symptoms estimated according to the Poisoning Severity Score was: none to mild (60.1%), moderate (14.0%), severe (11.2%), fatal (7.0%), and unratable (7.7%). The carboxyhemoglobin (COHb) concentrations, with poor correlation to symptoms, were less than 10% in 7.7%, between 10 and 30% in 26.6%, between 30 and 40% in 1.4%, higher than 40% in 0.7%, and unknown in 63.6% of all persons with COBIB. *Conclusion:* The number of COBIBs increased in Germany and Switzerland from 2000 to the end of August 2009. In most COBIBs two or even more persons were involved. Better information about the risk of indoor barbecues should be provided. *References:* 1. Gasman JD, Varon J, Gardner JP. Revenge of the barbecue grill. Carbon monoxide poisoning. West J Med 1990; 153:656–7.

185. Prevalence of Deaths in Acute Pediatric Poisoning: A 5-year Study

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Objective: To study the epidemiology of deaths due to acute poisoning in children in Bucharest and counties around. *Methods:* We have analyzed both cases registered in our department as well those investigated by the National Forensic Institute in a 5 year period, using medical documents and applying the following criteria: etiology, gender, age, residence, place of death. *Results:* Thirty-nine deaths of intoxicated children were registered between January 1st 2004 and December 31st 2008 i.e. 0.068% out of the total pediatric poisonings reported in this period in our centre. Out of the 39 cases 13 died in the hospital and 26 were found dead at home. Etiology of deaths was as follows: carbon monoxide in 13 patients (33.33%), pesticides in 8 situations (21%), drugs of abuse 6 children (16%), caustics 4 (10%), medicines 3 patients (8%), alcohols 2 (6%), gas 1 (3%), nitrites 1 (3%) and lead 1 (3%). The age distribution showed that the majority of the patients (17) were between 1–5 years followed by those over 12 years: 11 cases; 6–12 years: 6; and 0–1 year 5 cases. There were 24 boys and 15 girls reported in our statistics. *Conclusion:* Although the morbidity in acute poisoning in children is still high the mortality is relatively low, but of concern is the rate of deaths at home. The leading cause of death by poisoning in children has been shown to be carbon monoxide, source being the heating systems. Consequently the Poison Centre will have to attract the attention of the local authorities on this issue. *References:* 1. Trestrail III JH. Forensic Toxicology. In: Shannon M, Borron S, Burns M. Haddad and Winchester's Clinical Management of Poisoning and Drug Overdose. 4th ed. Philadelphia, USA: Saunders Elsevier Inc. 2007:119–25.

186. Trends in Hospitalisation due to Poisoning and in Telephone Enquiries to the Poison Control Centre Involving Slovenian Children and Young People

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Objective: To study the trends of hospital admissions secondary to poisoning in children and young people, and telephone enquiries to the Poison Control Centre (PCC) in order to identify priority areas for planning preventative measures. *Methods:* We searched the national hospital discharge database for injuries and poisonings from 1999 - 2008 in age groups 0 - 6 (AG1), 7 - 14 (AG2), 15 - 19 (AG3), and 20 - 24 (AG4) years. The agents were categorised into five groups according to the international disease classification codes[1] at discharge: medicines, alcohol, drugs of abuse, chemicals, and natural toxins. The PCC enquiry database was searched from 2004–2008 for the same age groups and agent categories. *Results:* An age specific rate of hospitalisations for all age groups and all agents except alcohol decreased from 734/100,000 inhabitants in 1999 to 487/100,000 inhabitants in 2008. Downward trends were identified in all age groups for intoxications with medicines (correlation coefficient, $R^2 = 0.5132$ in AG4), chemicals ($R^2 = 0.0295$ in AG4), drugs of abuse and natural toxins. Upward trends were identified for alcohol intoxications in all, but the youngest age group ($R^2 = 0.4227$ in AG2; $R^2 = 0.1001$ in AG3; $R^2 = 0.1715$ in AG4). In AG1 intoxications with medicines represented 39% of hospitalisations. In AG2 and AG3 the leading cause of hospitalisations was alcohol (43% and 52%), in AG4 medicines (42%). The number of enquiries to the PCC doubled, from 274 in 2004 to 468 in 2008. The main reason in AG1 was exposure to chemicals (49%); in the other three age groups exposure to medicines (42%-60%). Enquiries due to alcohol exposures were rare in all age groups (< 1%). *Conclusion:* The study identified a decreasing trend in hospitalisations due to intoxications in Slovenian children and young people, while the enquiries to the PCC doubled. The upwards trend in hospitalisations due to alcohol intoxication gives rise for concern and calls for urgent action. *References:* 1. World Health Organisation (WHO). International statistical classification of diseases and related health problems. 10th revision, ICD-10, Geneva, Switzerland, WHO, 1992.

187. A Prospective Study of the Incidence and Spectrum of Acute Poisonings in South Africa Based on Hospital Admission and Poison Information Centre Data

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Objective: The incidence and spectrum of acute poisonings in South Africa are unknown. A study was therefore conducted to establish the extent of the problem. *Methods:* A prospective study was conducted based on both Tygerberg Hospital admissions for acute poisoning and Tygerberg Poison Information Centre consultations over one year. Admission details were recorded and analysed for patient demographics, causes of poisoning and initial management of the patient. Poison centre consultation forms were analysed for similar data as well as interlocutor details and geographical distribution. *Results:* 662 patients were admitted to hospital. 78% were adults and 92% of these were intentional poisonings. Categories of exposures across all age groups were: medicines (76%), non-drug chemicals (26%) and biologicals (1%). Of the medicine related poisonings, paracetamol (27%) and amitriptyline (15%) were the most common. Cholinesterase inhibitors (18%) and paraffin (14%) were the most common non-drug chemical exposures. Mortality rate was 1%. The poison centre dealt with 5538 consultations of which 69% were from health care professionals. Forty-two per cent of the calls were received from the Western Cape Province and the remainder from elsewhere in South Africa. Fifty-six per cent of poison centre consultations concerned adults and of these, 61% were intentional exposures. Categories of poisoning exposures across all age groups were: medicines (35%), non-drug chemicals (53%) and biologicals (13%). Of the medicine related cases, paracetamol (16%) and benzodiazepines (9%) were the most common. Irritant/corrosive substances (28%) and cholinesterase inhibitors (10%) were the most common of the non-drug chemical exposures. *Conclusion:* The combination of data from hospital admissions and poison centre consultations provided important information with regard to the spectrum of poisoning exposures in the country. Intentional poisoning in adults and paracetamol ingestion were the most common entities in both sets of data. Medicine related poisonings were however most common in hospital admissions whereas non-drug related poisonings were the most common entity in poison centre cases. Although a combination of hospital admissions and poison information centre data is not necessarily a true reflection of the incidence and spectrum of poisoning, these are the only data sources presently available to us to indicate the extent of the problem.

188. Frequency and Severity of Paracetamol Poisoning Before and After Liberalization of Sale in Norway

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Objective: Before November 1, 2003 paracetamol was available only through pharmacies in Norway. A change in legislation was introduced in November 2003, allowing a range of pharmaceuticals, including paracetamol, to be sold outside pharmacies. We wanted to assess if this change in availability and sales outlet had affected the rate and severity of paracetamol intoxications in Norway. *Methods:* The following data for the years 2001–2002 and 2005–2006 (before and after change in legislation) were collected and compared: inquiries concerning paracetamol exposures to the National Poisons Information Centre (PIC), number of paracetamol related deaths (National Cause of Death Register), number of paracetamol related liver transplantations performed (the National Transplantation Unit), number of performed serum paracetamol analyses at selected hospitals (laboratory statistics), and sales statistics (the National Statistics of Drug Consumption). *Results:* The average number of paracetamol related inquiries to the PIC was 431 (124 assessed as potential severe) per year before the change in legislation and 744 (285 assess as potential severe) per year after the change. The increase in inquiries due to paracetamol exposure exceeds the overall increase in calls to the PIC. Paracetamol related deaths were 6.5 on average per year before and 7 after liberalization. Two paracetamol related liver transplantations were performed in 2005, one in 2006, and none in 2001 or 2002. Six out of eight hospitals had an increase in the number of serum paracetamol analyses. The total sale of paracetamol increased from 21.2 defined daily doses (DDD)/1000 inhabitants in 2001 to 27.3 DDD/1000 inhabitants in 2006, a 29% increase. The fraction of non-prescriptive packs sold from non-pharmacy outlets was 63% in 2006. *Conclusion:* The number of inquiries to the PIC due to paracetamol was significantly higher in 2005–2006 compared to 2001–2002. The number of paracetamol related deaths has not changed significantly. The increase in sale of paracetamol was mainly due to increased sale of prescription packages. Whether the increased number of paracetamol related inquiries to the PIC reflects a real increase in the incidence and severity of paracetamol overdose is not known. Studies on hospital admissions should be done to further assess this.

189. Frequency of Hyperbaric Oxygen Therapy and the Risk of Delayed Neuropsychiatric Effect Among Patients with Carbon Monoxide Poisoning

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Objective: Delayed neuropsychiatric syndrome (DNS) is a severe sequela that may develop after acute carbon monoxide (CO) poisoning. This study aims to investigate the risk factors for carbon monoxide-related DNS and the role of hyperbaric oxygen therapy for the delayed sequelae. *Methods:* A retrospective chart-review study was conducted and 516 cases enrolled with CO poisoning who had been admitted to

Taipei Veterans General Hospital between January 1990 and December 2007. Clinical characteristics were collected and analyzed. *Results:* Thirty-five cases developed DNS with an incidence of 6.8% during the 18-year period. Cases with carbon monoxide poisoning had been increasingly seen in recent years, mainly due to increase in intentional poisoning. Risk factors for DNS were age 34 years or older (odd ratio [OR], 3.5; 95% confidence interval [CI], 1.5–8.0; p = 0.004), intentional poisoning (OR, 4.9; 95% CI, 1.4–17.3; p = 0.0014), and presenting hypoxic encephalopathy (OR, 5.6; 95% CI, 2.3–14; p<0.001). Hyperbaric oxygen therapy was not beneficial in reducing DNS, whether the frequency was 1–3 times (OR 0.6, 95% CI 0.2–2, p = 0.4) or 4 times and more (OR, 0.98, 95% CI, 0.3–3.6, p = 0.98). *Conclusion:* Patients with acute CO poisoning who are aged 34 years or older, intentional poisoning and presenting hypoxic encephalopathy are high-risk groups for DNS. HBO_2 therapy is not warranted for reducing the delayed sequelae of CO poisoning.

190. Life Lost Due to Poisoning Premature Mortality in Morocco

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Objective: To measure premature poisoning mortality in Morocco according to age, and sex; and to quantify their economic loss to the society, in order to provide more information that can be used to develop and monitor health programmes that are aimed at reducing poisoning premature mortality. *Methods:* Potential economic losses were estimated by use of premature years of potential life lost (PYPLL), with a cut-off point at 65 years, and valued years of potential life lost (VYPLL) methods were applied for mortality data from 1990 to 2007. Variations in these measures were studied further in terms of age, sex, urban/rural residence, and socio-economic status. PYPLL rates for all leading factors of poisoning death have declined, using Moroccan sex-specific life expectancy for 2008 and age-specific weights of investment-producer-consumer model. *Results:* Of 1203 deaths, 1118 were under 65 years. The average of PYPLL was 41.6 years ± 14.8 years ranging from 1 year to 64 years. Male to female ratio was 1.1. It is shown that the average male to female ratio of PYPLLs is highest for accidental circumstances. The most incriminated products of PYPLL were pesticides, plants, gases, drugs and paraphenylene diamine. Among those, all the causes of poisoning death produced positive VYPLL, indicating a net loss to the society. *Conclusion:* Mortality rate only is an insufficient measure. The VYPLL seems to be an advantageous utility as an indicator of the economic impact and burden of premature poisoning deaths to society. In order to further reduce premature deaths, programs are required to improve the health of people living in rural areas. Targeted national programs are required to reduce avoidable deaths due to the several toxins implicated.

191. Maajoune Intoxication: Data Moroccan Poison Control Centre (1989–2007)

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Objective: Maajoune is a mixture very often consumed in Morocco and prepared from the resin of hemp and other aphrodisiac substances. The consumption of Maajoune can be deliberately for a feeling of wellbeing or for an aphrodisiac effect. Accidental ingestion was, in general, common in children.[1] The objective of our study is to determine the epidemiologic profile of the intoxication by Maajoune and particularly the circumstances of its consumption. *Methods:* Our study concerned cases of intoxication by Maajoune reported to the Poison Control Centre of Morocco (CAPM) during 19 years (1989 to 2007). All the cases were analyzed for demographic features, circumstances, clinical consequences, treatment undertaken and course of the poisoning and correlations between circumstances, age and sex. *Results:* 1098 cases were collected, accounting for 1.5% of all of acute poisonings. The average age of our patients was 20 ± 9.45 years, range 1 to 98 years. The sex ratio was 5.31 with 83.9% male and 15.7% female. The use of Maajoune as an addictive product was more frequent (54.2%). Accidental poisoning was most common in children (37.8%). Suicidal attempts occurred in 5.4% of the cases followed by criminal circumstance in 3%. These poisonings occurred frequently in the home (62.1%), less frequently in a public place (35.3%). The most commonly reported symptoms were neuropsychiatric (98%). The treatment advised by CAPM was symptomatic treatment (60%), gastric lavage in 8.2%. The outcome was favourable in 99.7% of the cases. However, three deaths were noted, probably related to the association of Maajoune with other substances. *Conclusion:* The use of Maajoune as addictive product has become more frequent in Morocco. The ignorance of its toxicity can have disastrous effects on health in the long term. *References:* 1. Bellakhdr J. La pharmacopée marocaine traditionnelle, Médecine arabe ancienne et savoirs populaires. 3rd ed. Rabat, Morocco: Ibis Press, 1997.

192. Scorpion Stings: A Public Health Problem in Beni Mellal (Morocco)

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Objective: The present study aimed at verifying the impact of a Moroccan strategy against scorpion stings through the analysis and interpretation of data recorded in the register. *Methods:* Our study is a retrospective study of scorpion stings based on medical charts of Beni Mellal. *Results:* From 2002 to 2006, 6,959 cases were registered in this province with an average incidence of 1.37%. The stings were more frequent in summer months, particularly July and August, and between 6 p.m. and 6 a.m. (60.2%). The average age of victims was 26.17 ± 18.38 years. Children were affected in 31.2% of the cases. Of all registered cases, 85.9% of the patients received medical aid in less than an hour after the sting. The envenomation rate (Class II and Class III) was 14.1% and the overall case-fatality rate was 0.5%. Statistical analysis of the various studied factors revealed a significant connection among the envenomation class (X^2 = 12.5; p<0.001), patient age (F = 3.8; p<0.001) and evolution. *Conclusion:* Scorpion stings remain a public health problem in Beni Mellal province. Further work is needed to provide a decrease in the lethality rate. *Acknowledgement:* This work is within PROTARS III D63/15 program and National Campaign for the control of scorpion stings and envenomation.

193. Valproate Overdose: A Retrospective Study of Self Poisoning

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Objective: To describe the epidemiology of valproate poisoning and the spectrum of its clinical effects, complications and treatments used. *Methods:* All patients were followed up by the Centre d'Assistance Médicale Urgente (CAMU) Tunis between January 2000 and October 2009. Consecutive valproate poisonings were identified with a supposed ingested dose greater than 3 g. *Results:* There were 65 patients with valproate poisoning from January 2000 to October 2009. The mean age of the studied population was 28 ± 10 years; the sex ratio was 44/21. At admission, nineteen patients had a GCS under 13, but 20 patients required mechanical ventilation with a mean duration of 72 ± 69 hours. Indication for intubation was coma in 18 cases and seizures in 2. The mean GCS was 12 ± 4. The mean supposed ingested dose was 13.7 ± 12.7 g in all patients, and 16.8 ± 8.5 g in ventilated patients. Patients consulted after a mean of 7.5 ± 8 hours. Seizures occurred in 6 patients. In 21 cases valproic acid was not the patient's medication. Activated charcoal was used in 41 patients. Four patients received L carnitine. Sixteen patients had metabolic acidosis consistent with severe valproate toxicity. In all patients mean lactate serum level was 3.4 ± 1.3 mmol/L and ammonium serum level is 61 ± 34 mmol/L, in ventilated patients 4.2 ± 1 mmol/L and 71.5 ± 18.3 mmol/L respectively. Massive ingested doses were directly related to decrease in conscious level (P<0.0001), and there was a significantly increased risk of mechanical ventilation (P = 0.03). In patients with chronic intake of valproate, repeated blood concentrations are required to determine the state of consciousness compared to patients with first contact with valproate; cut off: 408 vs 204 mg/L. *Conclusion:* Outcome was favourable for the majority of patients. There was one death directly related to massive valproate poisoning.

194. Reed Diffuser Toxicity

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Background: Air fresheners have become increasingly popular over recent years with marketing aimed at removing odours, refreshing the air and creating a pleasant ambient mood. Their popularity has resulted in a multi-million pound market with new products continually being released. Air fresheners come in many forms including sprays, plug-ins, gels and candles. Due to their wide use and availability, ingestion of these products is common with hundreds of cases being reported to the National Poisons Information Service (NPIS) annually. Whilst many air-fresheners contain potentially harmful products, they are usually difficult to ingest in large amounts and serious effects are therefore uncommon. Recently however, the NPIS has seen the emergence of a new type of air freshener which has led to concern. Reed diffusers, although available for many years, have seen a massive surge in popularity in 2009. They are usually composed of a bottle filled with approximately 100 - 500 mL of scented liquid delivered to the room by "wicking" reeds made of bamboo or similar. Some also contain decorative items such as beads. The liquid is easily accessible due to the open neck of the bottle and therefore has potential to be ingested in large quantities. The ingredients of reed diffusers vary dramatically. A small sample of different products revealed a contents list which can include 90% essential oils; 85% glycol ethers; 80% ethanol or 78% hydrocarbons. *Case series:* From January to November 2009 the NPIS (Cardiff) has received 27 calls involving reed diffusers. These all involved young children aged between 8 months and 4 years with an average age of 21 months. One enquiry involved eye contact, four involved ingestion of beads or pearls from within the unit and 22 involved ingestion of the liquid itself, most of these cases involving unknown amounts. *Conclusion:* These products are of serious concern due to the ease with which young children may ingest significant quantities of potentially life threatening compounds. It is essential that health professionals are aware that the reed diffuser type of air freshener is not as innocuous as those with which we are more familiar and that all cases should be treated as potentially serious.

195. Toxicity of Essential Oils

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Objective: To describe the epidemiology of essential oil poisoning reported to the National Poisons Information

Service (Cardiff) and to review the toxicity of essential oils. *Methods:* Interrogation of the United Kingdom Poisons Information Database (UKPID) and literature review using Medline. *Results:* Of 92,731 exposures reported to the NPIS (Cardiff) from Jan 2004 to January 2008, 1518 (1.6%) involved essential oils. Of these cases, 1280 (84%) were ingestions. Most exposures (66.0%) involved patients under the age of 4 years. A review of the literature suggests that certain essential oils (eucalyptus, pennyroyal, turpentine and clove) are more commonly encountered in human exposure. It is not clear whether this is due to greater toxicity or wider use of these particular oils. It is generally regarded that certain oils (pennyroyal, tea tree, turpentine, wintergreen, and wormwood) are too toxic to be used in aromatherapy. Others such as lavender oil are thought to have a much lower toxicity.[1] Toxicity from essential oil ingestion (and less commonly dermal contact or intravenous injection) includes gastrointestinal upset, central nervous system depression, aspiration pneumonitis, hepatic and renal failure.[2–4] Although the data are limited, it has been suggested that there may be distinct patterns of toxicity for individual oils, e.g. hepatotoxicity with pennyroyal and clove oils. *Conclusion:* Although toxicity from essential oil exposure is rarely encountered, severe toxicity has been reported in the medical literature. Essential oils are widely available in many over the counter preparations in the United Kingdom. It is therefore important to remain vigilant to the risks associated with essential oil exposure. *References:* 1. Lis-Balchin M. Aromatherapy Science. A guide for healthcare professionals. 1st ed. London, UK: Pharmaceutical Press 2006. 2. Tibballs J. Clinical effects and management of eucalyptus oil ingestion in infants and young children. Med J Aust 1995; 163:177–80. 3. Troulakis G, Tsatsakis AM, Astrakianakis A, et al. Acute intoxication and recovery following massive turpentine ingestion: clinical and toxicological data. Vet Human Toxicol 1997; 39:155–7. 4. Eisen JS, Koren G, Juurlink DN, et al. N-Acetylcysteine for the treatment of clove oil-induced fulminant hepatic failure. J Tox Clin Tox 2004; 42:89–92.

196. Calls to the National Poisons Information Service (Cardiff) from 2005 to 2009 Involving Tramadol, Compared with Other Opioid Analgesics, Toxbase© Hits and Rates of Prescribing in England and Wales

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Objective: To investigate poisoning with opioid analgesics over a six year period using call data from NPIS (Cardiff), comparing results with prescriptions in the community. *Methods:* Records of all enquiries made to NPIS (Cardiff) between January 2004 and October 2009 were reviewed. Calls related to patients involving opioid analgesics were counted. Prescription rates were obtained from Prescription Cost Analysis Data for England[1] and Wales[2]. *Results:* Table 1 shows a summary of results. Call figures are given as percentage of total calls involving opioid analgesics. Calls involving tramadol have increased from 11.7% of total opioid analgesics to 18.8% over the six year period. Coproxamol enquiries have decreased from 18.2% to 0.5% and codeine has increased from 36.2% to 50.7%; oxycodone increased from 0.6% to 1.9% and dihydrocodeine decreased from 22.5% to 14.2%. The number of TOXBASE© hits for tramadol increased from 0.66% of total hits to 1.14%. *Conclusion:* Both NPIS enquiries and prescriptions for coproxamol have fallen since its withdrawal in 2005. No single opioid appears to have been used as a substitute analgesic. There was a marked increase in calls to NPIS (Cardiff) regarding all other opioids including tramadol with the exception of dihydrocodeine which has decreased steadily since 2004. Use and overdose of tramadol should be monitored closely over coming years due to the potential for significant neurological toxicity. *References:* 1. Prescription Cost Analysis 2004–2008. NHS Information Centre 2009. 2. Prescriptions Dispensed in the Community, 2000 to 2008 and Prescription Cost Analysis (PCA) Data. Welsh Assembly Government 2009.

197. Meprobamate and Cardiotoxic Drug Poisoning Admitted to Intensive Care Units

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Objective: The aim of this study was to assess characteristics of meprobamate and cardiotoxic drug poisoning in a teaching hospital. *Methods:* All patients admitted to Intensive Care Units (ICU) over a six-month period for acute poisoning with meprobamate or cardiotoxic drugs were included in this retrospective cohort study. Information (including that on stated dose ingested, organ failure before and at admission, ECG and hemodynamic parameters) was extracted from case notes. *Results:* 172 patients were admitted to ICUs for acute poisoning and 51 (30%) had ingested meprobamate or other cardiotoxic agents. Among the 51 patients, 60% had ingested meprobamate and 40% other cardiotoxic drugs. Median age was 44 (17–84) and 61% were female. In 20% of cases, patients had known underlying cardiovascular disease. Patients ingested cardiotoxic drugs with membrane stabilizing activity in association with other drugs in 59% of cases. In all cases of shock but eight, supposed dose ingested was higher than toxic dose. Cardiogenic shock was proven in 40% of cases at admission to ICUs. In four cases, patients were in refractory cardiac arrest when they arrived at hospital. For all but four patients, supportive treatments and supplementation of failing organs were efficient. In all cases, fluid challenge was initiated before admission to ICUs and then positive inotropic agents or vasopressors were used to treat shock in 21 cases. Twenty three patients were mechanically ventilated for a mean duration of 4.8 days. Patients with underlying cardiovascular disease or who had ingested many cardiotoxic drugs in association were sicker than others. Four patients presented with prolonged cardiac arrest with refractory shock following a drug overdose and not responding to optimal conventional treatment. Two of these have been referred to cardiac surgery for extracorporeal life support. Finally, two patients died in medical ICU. *Conclusion:* Poisoning with meprobamate and cardiotoxic drugs constituted 30% of all poisonings admitted to intensive care. Patients with underlying cardiovascular disease or who had ingested many different drugs were sicker than others. Earlier transfer towards cardiac ICU could improve outcome of patients who presented to medical ICU with refractory shock.

Table 1. Enquiries to NPIS (Cardiff) involving opioid analgesics, number of prescribed items in England and Wales, and TOXBASE© hits for tramadol, 2004–2008 and NPIS enquiries for Jan–Oct 2009

		Year					
		2004	2005	2006	2007	2008	2009 (10 mth)
Tramadol	% of total opioid analgesic enquiries	11.7	13.3	14.3	13.8	17	18.8
	Total prescribed items (1000s)	3450	4234	4917	5478	6121	
	TOXBASE© hits (% of total)	0.66	0.76	0.86	0.94	1.14	
Coproxamol	% of total opioid analgesic enquiries	18.2	13	6	3.6	1.7	0.5
	Total prescribed items (1000s)	7795	3148	1444	979.6	391.8	
Codeine (inc. cocodamol)	% of total opioid analgesic enquiries	36.2	37.8	44.4	44.9	49.2	50.7
	Total prescribed items (1000s)	13244	15485	16572	17685	18715	
Dihydrocodeine (inc. codydramol)	% of total opioid analgesic enquiries	22.5	22.1	19	16.9	16.2	14.2
	Total prescribed items (1000s)	6623	7125	6957	6787	6599	
Oxycodone	% of total opioid analgesic enquiries	0.6	0.8	0.8	1.5	2.1	1.9
	Total prescribed items (1000s)	226.7	319.8	417.6	539.1	672.6	

198. A Poisoning and Prescribing Data Analysis for Mefenamic Acid

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Objective: Mefenamic acid is used commonly to treat dysmenorrhoea and is therefore often available to female adolescents, a high risk group for self poisoning.[1] Although most non-steroidal anti-inflammatory drugs (NSAIDs) are of low toxicity, mefenamic acid overdose may be associated with convulsions in up to 38% of cases.[2] This is much more common than with other NSAIDs (<2%).[3] Since there is no evidence that mefenamic acid is more efficacious in the treatment of dysmenorrhoea than other NSAIDs,[4] its use has been discouraged for this indication. This study was therefore performed to examine the trends in prescribing and overdose of mefenamic acid. *Methods:* Data analysis of calls received by the UK National Poisons Information Service (NPIS), accesses to TOXBASE® and National Prescription Prescribing Authority data between April 2004 and March 2009. *Results:* Over the 5 years of study there was a small but statistically significant ($p<0.0005$) decline in prescriptions. However, TOXBASE® hits for mefenamic acid and the number of calls to the NPIS remained unchanged. A total of 1018 calls were received during the 5 year period, 71% of which related to self harm; 81% involved females and in 46% the age range was 15 to 25 years. *Conclusion:* As expected, a large proportion of overdoses involve young females and frequency has not been reduced in spite of modest reductions in prescribing. Further efforts are required to discourage prescribing of mefenamic acid, especially for those at high risk of self harm. *References:* 1. Vale JA, Meredith TJ. Acute poisoning due to non-steroidal anti-inflammatory drugs: clinical features and management. Med Toxicol 1986; 1:12–31. 2. Balali-Mood M, Critchley JA, Proudfoot AT, et al. Mefenamic acid overdosage. Lancet 1981; 2:1354–6. 3. Bialas MC, Reid PG, Routledge P, et al. Changing patterns of self-poisoning in a UK health district. Q Med 1996; 89:893–901. 4. Marjoribanks J, Proctor ML, Farquhar C. Nonsteroidal anti-inflammatory drugs for primary dysmenorrhoea. Cochrane Database Systematic Review 2003; 4:CD001751.

199. Hospital Mortality Owing to Chemical Poisonings in Azerbaijan 2004–2008

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Objective: The epidemiology of lethal poisoning cases in Azerbaijan is still uninvestigated. *Methods:* We analyzed data of fatal outcomes in patients admitted to ICU of the Republican Clinical Toxicology Center MoH, Baku, Azerbaijan from 1st January 2004 through 31st December 2008. *Results:* The total number of fatal poisonings was 195 or 3.2±0.19% of admitted patients. There were 137 males (70.3%) and 58 females (29.7%). The age range was from 1 to 84 years (mean ± SD = 39.2±20.9 years). Most of the fatalities were seen in the age range 40–49 years (21.0%). The childhood group

(age <15 years) was 10.3%. The most frequent cause of death was ingestion of corrosives (30.8% of total mortality) and especially concentrated acetic acid poisonings. All these cases were suicide attempts. The other lethal poisoning cases were alcohol intoxications (19.5%) followed by pharmaceutical poisonings 12.3%, intoxication by narcotics 7.7%, inhalation of carbon monoxide 7.2%, envenomation by snake venom 5.6%, organic solvent intoxications 4.6%, poisoning by organophosphates 4.1%, acute toxic-allergy reactions (Lyell's syndrome and others) 2.6%, mushroom poisonings 2.1%, poisoning by arsenic and its compounds 0.5%, "black widow" spider venom intoxications 0.5% and the toxic effect of unspecified substances 2.6%. *Conclusion:* Corrosive liquid poisonings were the prime causes of mortality due to acute chemical intoxications in Azerbaijan Republic. The unrestricted sale of concentrated acetic acid in Azerbaijan must be banned.

200. Epidemiological Characteristics of Hospitally Treated Poisonings in 1988 and 2008 Year at the University Clinic of Toxicology, Skopje

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Objective: The transitional period in developing countries influences the dynamics and causes of poisonings. The objective of the study is the estimation of poisoning pattern differences in hospital treated patients in the years 1998 and 2008. *Methods:* The recorded data of all patients hospitalized at the Clinic of Toxicology were analyzed. Patients who were ambulatory with mild poisoning clinical presentations were not included in the study. *Results:* There was an increase in the rate of poisonings in males from 1998 to 2008 (34.1% to 45.4%), no significant difference in suicidal attempts (73.1% to 75.6%) and lethal outcome (3.12% to 3.11%). Caustic poisonings increased by about 1% (15.3% to 16.5%) but poisonings with benzodiazepines increased almost twice (38.4% to 57.5%). Mushroom poisoning decreased (7.58% to 3.64%). There was no statistical difference in sex distribution of suicidal poisonings between 1998 and 2008 ($r = 0.152$, $p = 0.001$ to $r = 0.193$, $p = 0.000$). Higher lethal outcome in older patients is registered in each year ($r = 0.234$, $p = 0.000$ to $r = 0.127$, $p = 002$) with no significant difference in the average age of the patients (32.1±15.6 to 34±16.4 years). The length of hospital treatment also decreased (6.26±8.25 days to 4.12±4.36 days). There were no severe poisonings with paracetamol in this 10 year period. *Conclusion:* There was an increased number of poisonings in males and poisonings with pharmaceuticals during the 10 year transitional period. A decreased number of pesticide poisonings is mostly related to factory closing and lower economic standard of living with no storing of pesticides. Caustic poisonings maintain the trend due to the easy availability and low prices of the products. The shortening of hospital stay is related to the improvement in poisoning treatment.

201. Cannabinoid Intoxication Patient Presentations to US Emergency Departments

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Objective: Cannabinoids are one of the most frequently abused hallucinogens in the US, but acute intoxications rarely present to hospital emergency departments (EDs). Cannabinoid intoxication in ED patients is poorly studied. The purpose of this study was to characterize cannabinoid intoxications presenting to New Jersey and New York emergency departments. *Methods:* Design: A multi-center retrospective emergency department (ED) cohort. Study setting: 20 New Jersey and New York EDs. Subjects: Consecutive patients with the ED diagnosis of poisoning hallucinogenic agent, (ICD10 code = T40.7) or cannabis abuse (ICD10 code = F12) were identified from October 1, 2008 to September 30, 2009. Only completed charts with documentation of an acute single intoxication with cannabis were included. *Results:* Out of 1,590,248 consecutive patients, there were 326 charts with matching ICD10 codes. Eighty-four patients met inclusion criteria and were included in the study (0.0053% of all ED patients). The patient demographics were as follows: mean age = 20.5 years (range: 14–42 yrs), gender = 61% males. Nineteen per cent of patients admitted their ED presentation was their first usage of a cannabinoid. The most commonly reported symptoms were: "anxiety," "palpitations," "shaking," "paresthesias," "dizziness," and "nausea." Acute hallucinations were reported by 4 patients (4.8%), and acute agitation or psychosis was observed in 7 patients (8.3%). Only 1 out of 84 enrolled patients (1.2%) was admitted to the hospital for a complaint of persistent dyspnea. All patients received symptomatic treatment only. There were no recorded deaths in the ED. *Conclusion:* Cannabis intoxication is a rare presentation to US emergency departments. Toxic effects appear to be mild and self-limiting. Many ED presentations for acute cannabinoid intoxications occur following the first usage of this illicit drug.

202. Methadone Overdose Patients Presentations to US Emergency Departments

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Introduction: Methadone overdose is an infrequent type of opioid poisoning presentation to US emergency departments (EDs). Compared to other opioid poisonings, methadone is particularly dangerous because of its prolonged duration of action. The epidemiology of methadone overdoses to US EDs is poorly studied. *Objective:* To characterize methadone overdoses presenting to New Jersey and New York emergency departments. *Methods:* Design: A multi-center retrospective emergency department (ED) cohort. Study setting: 20 New Jersey and New York EDs. Subjects: Consecutive patients with the ED diagnosis of methadone poisoning (ICD10 code = T40.3) were identified from October 1, 2008 to September 30, 2009. *Results:* Out of 1,590,248 consecutive patients, 64 patients were diagnosed with methadone poisoning (0.004% of all ED patients), but only 40 had completed charts for review. The patient demographics were as follows: mean age = 39.7 years (range: 16–62 years), gender = 50%, mean methadone dose = 78 mg (range: 30–140 mg). Overdoses were more frequent on Monday (18%), Thursday (18%), and Friday (20%). The poison center was notified and naloxone was administered in 5% and 27.5% of cases, respectively. Hospital admissions occurred in 28% of patients and were due to prolonged sedation or unrelated complications. There were no recorded deaths or intubations in the ED. *Conclusion:* Methadone poisoning is a rare presentation to US emergency departments. The risk of mortality and serious morbidity (e.g. intubation) appears to be extremely low.

203. Is There an Association with Methemoglobinemia and Carbon Monoxide Poisoning?

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Introduction: Methemoglobinemia (Methgb) is a condition in which the iron within hemoglobin is oxidized from ferrous to the ferric state, leading to variable degrees of deficiencies in oxygen transport. There is limited data regarding acquired Methgb and its association with carbon monoxide (CO) poisoning. *Objective:* To determine the incidence of Methgb in patients who have been exposed to carbon monoxide. *Methods:* Design: Multi-center retrospective cohort study. Setting: 23 NJ/NY EDs. Subjects: Consecutive patients with the ICD-9 diagnosis of "toxic effects CO" from January 2000 to October 2006. A manual chart review was performed to determine which patients had Methgb levels. Patients without documented Methgb levels were excluded. A serum Methgb of more than 1% was considered abnormal. Statistics: Mann-Whitney with preset alpha of 0.05. *Results:* "Toxic effects of CO" was diagnosed in 1131 patients. Ninety patients (8%) met inclusion criteria. Mean age was 34.5 years (±20 SD). Twenty-one were < 18 yrs of age. Fifty-three per cent were female. Seven per cent (n = 6) were admitted and 2% were transferred (n = 2). Four patients were treated with hyperbaric oxygen. Mean overall Methgb level was 0.75%. An elevated Methgb was determined in 8 patients (range 1.2–15%). Mean COhgb level was 5% in those with methemoglobinemia, compared to 5.4% in those without ($p = 0.46$). One patient with methemoglobinemia was admitted (car fire in garage), whose level was 15%. *Conclusion:* Only a small number of patients with CO exposure have elevated Methgb levels. The incidence of Methgb does not correlate with COhgb levels.

204. Not Only Good Wine . . . The Impact of Acute Intoxications in Toxicology Unit Care in North East Italy

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Objective: This was a retrospective hospital based study performed with the purpose of investigating the epidemiology of acute intoxication (AI), and performed in a Toxicology Unit Care (TUC) in an Emergency Department (ED) (TUC/ED) in Verona, Northern Italy during the year 2009. *Methods:* All data regarding subjects who presented to the TUC/ED with a diagnosis of definite or suspected acute intoxication and poisoning were collected from its database. To extract patients some key words such as "poisoning", "acute intoxication", "bleach", "ammonia", "mushrooms" and "ingestion" were used. All alcohol and carbon monoxide related AI cases were excluded. *Results:* 244 cases were analyzed: 45.9% males and 54.9% females, mean age respectively 45.1 and 43.9 years. The distribution of admitted patients remained fairly constant, except for a slight rising prevalence in autumn (poisonous mushroom ingestion) during the year, with a majority of yellow (45.9%) and green (43.4%) triage codes. Only 1.6% of females and 1.2% of males showed a severe symptomatology already on admission. The pattern of exposure was: ingestion (82.7% of cases; two major age peaks: 18–34 and 35–51 years of age) mostly due to food - such as mushrooms, drinks, detergents, soap, pharmaceuticals, drugs of abuse; caustic substances: contact (10.2% of cases; age peak 18–51); and inhalation (6.9% of cases). In 17.2% of cases the poisoning exposure was intentional. In 63.5% of cases the patients were sent to their general practitioners (45.5% of the yellow and 81.1% of the green coded patients) and in 22.1% of cases they were admitted to clinical rooms (44.6% of the yellow coded patients). Considering only admitted patients 92.6% of them were coded yellow. *Conclusion:* In most cases the triage codes assigned to the patients admitted to the studied TUC/ED were yellow or green. Considering that the seriousness of the symptoms can appear several hours after the exposure to toxic substances, a quick and a specific intervention to obtain the most effective treatment is appropriate, in order to save lives and avoid irremediable health damage.

205. Monitoring Caustic Injuries from Emergency Department Databases Using an Automatic Keyword Recognition Software

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Objective: In Italy the EU Injury DataBase (IDB) reports the involvement of chemical products in 0.9% of

home and leisure accidents.[1] The whole European sample reports a similar figure for injury by chemicals and 0.2% for chemical corrosion injuries.[2,3] A simplified ED registry on home accidents (SINIACA) and the Poison Control Centres record injury and poisoning cases.[4,5] Ninety per cent of toxic exposures occur at home. The effects of chemical agents are frequently observed in hospitals and have a high potential risk of damage, with double the rate of hospital admission for home injuries, especially for caustic exposures. The aim of this study is to monitor caustic effects in Italy using automatic recognition of free-text in ED medical databases. *Methods:* We created a Stata software program to automatically identify caustic or corrosive injury cases. The procedure has to recognize caustic or corrosive agent within the free text using an agent specific list of keywords. In order to assess the capacity of recognition of this expert system we focused attention on the sensitivity and specificity of the procedure. We checked the validity of the system by direct manual quality control on free-text description for the selected cases and for all those codified as chemical/thermal agent effect or poisoning/intoxication. *Results:* 10 hospitals from 6 regions participated in the study. The program identified 112 cases of injury by caustic or corrosive agents. Checking the cases for quality control we assessed 99 cases as true positive cases, that is to say 0.59% (99% CI: 0.45-.76) of the total sample, almost 3 fold greater than the expected value ($p<0.000$) from European codified information. False positives were 11.6% of the recognized cases (99% CI: 5.1%-21.5%). *Conclusion:* Our automatic procedure for caustic agent identification proved an excellent system for product recognition with an acceptable level of sensitivity. Contrary to our *a priori* hypothesis the automatic recognition presented a level of individuation of agents with caustic effects significantly greater than what was expected according to the values from current codifications reported in the European database. *References:* 1. Pitidis A, Gallo L, et al. The injury database (IDB) in Europe, surveillance of home and leisure accidents: Italy 2005. Rapporti ISTISAN 08/45: Italian National Institute of Health, 2008. 2. Angerman A, Bauer R, et al, Injuries in the European Union. Summary 2003–2005. The EU Injury Database, 2007. 3. Lyons RA, Polinder S, Larsen CF, et al. Eurocost Reference Group. Methodological issues in comparing injury incidence across countries. Int J Inj Contr Saf Promot 2006; 13:63–70. 4. Pitidis A, Taggi F. Ambiente casa: la sicurezza domestica dalla conoscenza alla prevenzione. FrancoAngeli editore, 2006. 5. Settimi L, Davanzo F, Carbone P, et al. Surveillance of toxic exposures: the pilot experience of the Poison Control Centers of Milan, Pavia and Bergamo in 2006. Ann Ist Super Sanità 2007; 4:287–94.

206. Poisoning Risk Caused by Cosmetic Products

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Objective: Cosmetic exposures are frequent causes of poisons centres' (PC) inquiries. Overall product safety is considered as high. Based on the forthcoming new EU cosmetics regulation a Cosmetic Products Notification Portal (CPNP) providing access to formulations of all cosmetics marketed in the EU for European poisons centres will be installed with substantial expenditure. This study is directed at quantifying the poisoning risk caused by cosmetics. *Methods:* All exposures to cosmetic products reported to the authors' poisons centre between 1999 and 2008 were selected from the PC case database. Cases were analysed for groups of agents involved and poisoning severity. An 'IntoxIndex' was calculated for all agent groups, by dividing the sum of all moderate, severe or lethal poisonings, by the number of all exposures. *Results:* Within the study decade 12,575 exposures to cosmetic products were identified corresponding to 4.8% of all exposures recorded. In 71.8% no symptoms, in 20.6% minor symptoms were reported; 0.8% of all cases were considered as moderate or severe. There were 6 lethal cases, including one case of questionable relationship to exposure (severity not evaluated: 6.7%). The overall IntoxIndex was calculated as 0.9%. Table 1 breaks down the cases to agents involved indicating that most cases were reported for skin care products, while hair colouring agents were the product group with the highest poisoning risks (IntoxIndex = 2.1%). *Conclusion:* Cosmetics are comparably safe, but some serious and even lethal poisoning occurs that may indicate the need for access to cosmetic formulations in daily PC work.

Table 1. IntoxIndex for cosmetics

Severity:	lethal	severe	moderate	minor	no symp.	unknown	sum	IntoxIndex
hair colouring agents		1	3	67	92	26	189	2.1%
hair shampoo		1	12	324	1491	87	1915	0.7%
other hair care products			8	120	320	35	483	1.7%
all hair care products		**2**	**23**	**511**	**1903**	**148**	**2587**	1.0%
bathing additives	1	1	12	258	906	83	1261	1.1%
skin cream		2	3	191	902	54	1152	0.4%
liquid deodorant	2	1	3	130	250	39	425	1.4%
soaps	2	2	12	230	1154	68	1468	1.1%
other skin care products			13	568	1891	175	2647	0.5%
all skin care products	5	6	43	1377	5103	419	6953	0.8%
dental cleaning products	1		4	242	743	88	1078	0.5%
nail care products		5	15	374	811	111	1316	1.5%
other cosmetic products		1	4	89	473	74	641	0.8%
all cosmetic products	**6**	**14**	**89**	**2593**	**9033**	**840**	**12575**	**0.9%**

207. Prospective Study on Poisoning Risk Caused by Transfer of Hazardous Agents to Beverage Containers

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Objective: It is well known from poisons centres' work that ingestion of hazardous agents from water bottles or beverage cans by mistake causes chemical burns and poisonings. A lethal poisoning related to ingestion of decanted cleaning products reported to the authors' poisons centre in 2007 initiated a study to evaluate the frequency and severity of such events to provide a basis for preventative action. *Methods:* The study includes all exposures reported to the authors' poisons centre from July to September 2009, restricted to cases where patients mistake hazardous agents for beverages or food because they had been decanted into food-like containers. All exposures that satisfied inclusion criteria were identified and checked for completeness of data set and followed up by telephone interview within 48 h. *Results:* Within 10,520 recorded exposures, 53 cases (0.5%) fulfilled the inclusion criteria. In 28 cases the agent was identified, in 25 cases not. Thirteen patients were exposed to professional products, 4 were exposed to products for professional and household use, 27 to household products (9 unknown). Thirty patients drank liquids out of bottles intended to be used for beverages, 5 out of cans, and 5 out of other food like containers (13 unknown). Twenty-three exposed patients were younger than 19 years while 30 were older. Forty one exposures occurred at home, a group of 7 was exposed in an open air bath (5 in other locations). Forty-nine patients had ingested the product while 4 patients had inhaled it. Twenty-four patients had no symptoms, 13 minor, 14 moderate, 1 severe (1 unknown). Thirty-eight patients were treated by medical professionals. A frequency of 1.5 reported mistakes per 100,000 inhabitants per year satisfying the study criteria was calculated from these results. *Conclusion:* The proportion of moderate or severe poisonings in this series is 28.3%, while the proportion of moderate or severe poisonings for all chemical product exposure cases reported to the authors' poisons centre within the last decade is only 2.1%. Thus, transfer of hazardous products to beverage containers is a frequent cause of exposure by mistake, leading disproportionately often to serious poisonings with need for medical treatment.

208. Analysis of the Self-harm Cases Received at Al-Watani Governmental Hospital In Palestine

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Objective: To analyze the self-harm and suicidal poisoning cases which were received at Al-Watani Governmental Hospital in Palestine during the previous year from May 2008 - April 2009. *Methods:* All poisoning cases that were received at Al-Watani hospital/emergency department that resulted from self-harm or suicide were included. Demographic and clinical information about the cases was collected, entered into SPSS, and analyzed. *Results:* A total of 54 cases were included, the majority of the self-harm patients were female (35 cases [64.8%]). Most self-harm patients were adults, with 13% occurring at age 18, and 11% occurring at age 24. Most poisoned patients were living in cities (57.4%), and a lesser percentage was living in villages (31.5%), or camps (9.3%). Most self-harm cases were carried out using medications (70.4%), others with pesticides, cleaning products, or other products. Most cases involved a single ingestion (75.9%), while multiple ingestions were used in the rest. Only hours had passed before the poisoned patients decided to seek medical help in the majority of cases (44.4%), others did not specify the time of exposure to the poison(s). Oral ingestion was the route most commonly used (98.1%), and injection was used to a much lesser per cent. Regarding the decontamination, lavage was performed for 42.6% while only 7.4% received activated charcoal, and 11.1% had both. *Conclusion:* This is the first article that sheds light on such a sensitive issue in a country plagued by instability. The government needs to take further action on this issue in order to better help and protect citizens with depression or hardship. Continuous medical education is sorely needed for physicians treating self-harm patients. Support groups and psychological support should also be incorporated in order to better help patients.

209. Occupational Exposure to Epibatidine Associated with Widespread Vesicular Rash

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Objective: Epibatidine is a highly potent nicotinic receptor agonist and has been used to explore the physiological and pharmacological basis of several diseases.[1,2] The chemical name is exo-2-(6-chloro-3-pyridinyl)-7-azabicyclo[2.2.1]heptane hydrochloride and CAS number 140111–52-0. Previous human exposure has not been described. We report a case of inadvertent occupational exposure in a previously healthy young man. *Case report:* A 25-year-old laboratory worker had been preparing a batch of dilute samples from a concentrated sample of epibatidine hydrochloride (Tocris Bioscience, Missouri, US) for around 2 hours. He had been wearing protective gloves and laboratory clothing but his face was unprotected. Around 30 minutes after completing this task he developed an intense itch affecting upper and lower limbs and trunk.

On arrival at hospital he was noted to have past history of asthma that was well controlled, and had no previous skin disorder. He was taking no regular medications. Examination found a vesicular rash overlying the extensor surfaces of the forearms, around both axillae, and both calves. There was sparing of mucous membranes and no lymphadenopathy. Resting electrocardiograph showed sinus bradycardia (HR 49 per min) and was otherwise normal. Serum electrolytes, liver biochemistry, C1 esterase inhibitor, complement C3 and C4, anti-neutrophil cytoclastic antibody PR3 and MPO, immunoglobulin E were within normal limits. Immunoglobulin G was marginally elevated at 13.7 g/L (reference range 5 to 13 g/L), and subfractions 1 to 4 were within normal limits. A single dose of oral prednisolone 40 mg was administered followed by regular oral chlorpheniramine 4 mg thrice daily. At 24 hours the vesicular rash persisted but itch had significantly lessened and the patient was discharged from hospital. One week later, the vesicular rash was noted to have resolved. *Conclusion:* A causal relationship was supported by the close temporal relationship between exposure and rash and lack of an alternative cause. There was uncertainty as to whether exposure had been dermal or inhalation; nonetheless, the distribution of rash indicated a systemic rather than localised reaction. *References:* 1. D'hoedt D, Bertrand D. Nicotinic acetylcholine receptors: an overview on drug discovery. Expert Opin Ther Targets 2009; 13:395–411. 2. Daly JW. Nicotinic agonists, antagonists, and modulators from natural sources. Cell Mol Neurobiol 2005; 25:513–52.

210. Accidental Intravenous Chlorhexidine Digluconate Causing Unconsciousness

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Objective: There are few reports in the literature on the clinical effects of intravenous chlorhexidine injection. Accidental i.v. administration of small amounts of chlorhexidine is usually relatively benign. However, intravenous administration of 800 mg chlorhexidine gluconate resulted in hypotension, tachycardia, and acute respiratory distress syndrome in one patient.[1] We present a case of i.v. injection of 100 mg chlorhexidine. *Case report:* A 79-year-old man with chronic renal disease on warfarin treatment received a bolus of 20 mL of 0.5% chlorhexidine digluconate in ethanol 56% (100 mg chlorhexidine digluconate) by accident during preparation for hemodialysis. In less than one minute he felt ill with a warm feeling in his head and he lost consciousness. When he woke up in less than a minute he felt warm and unwell. His blood pressure was 192/62 and the heart rate 57. He improved in half an hour. Hemodialysis treatment was performed without any complications for four hours as planned. After the dialysis the patient wanted to return to his home for the night. The next day he was in good condition and his chest x-ray and laboratory results were normal. *Conclusion:* Intoxication with 100 mg chlorhexidine resulted in transient loss of consciousness. The clinical course was uneventful after performing a planned hemodialysis. The influence of hemodialysis on the clinical course is however unsure. *References:* 1. Ishigami S, Hase S, Nakashima H, et al. Intravenous chlorhexidine gluconate causing acute respiratory distress syndrome. Clin Toxicol 2001; 39:77–80.

211. Therapeutic Errors Involving Ingestion of Clotrimazole Pessaries by Women

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Objective: Since 2004 in Australia, the number of over the counter treatments for vulvovaginal candidiasis has increased, with single dose oral fluconazole joining intravaginal clotrimazole as available from the pharmacist without prescription. In more recent years, combination packs of single clotrimazole pessary plus external clotrimazole cream and single dose oral fluconazole plus external clotrimazole cream have also been released. This study aimed to investigate if the increased over the counter availability and marketing of products to treat vulvovaginal candidiasis has led to increasing rates of women accidentally ingesting vaginal pessaries in Australia. *Methods:* A retrospective review of calls made to the NSW Poisons Information Centre in the time period 2004–2009 involving females aged 12 years or older accidentally ingesting a clotrimazole pessary. *Results:* There were 268 therapeutic errors matching the search criteria in the time period examined. There were 5 in 2004, 23 in 2005, 36 in 2006, 42 in 2007, 69 in 2008 and 93 in 2009. Age ranged from 16 to 82 (specific age recorded for 32 exposures only). Eleven females had presented to hospitals following ingestion and 13 saw a general practitioner for advice. There were 17 women who reported possible minor symptoms related to the exposure at the time of the call: eight complained of nausea, three of vomiting, three of flushing, one of widespread skin rash, one of abdominal pain, one of lip swelling, one of shaking, one of headache and one of weakness. Of the 35 ingestions reported with strength, 26 were 500 mg once only pessaries and nine were 100 mg six day pessaries. *Conclusion:* There has been a sharp increase in the rates of accidental ingestion of clotrimazole pessaries since 2004 in women. The range of products available and increased marketing of oral products in Australia has likely contributed to confusion for women. Pharmacists and physicians are reminded to provide adequate counselling on the use of these products and ensure they are supplying the intended product. Manufacturers should also consider revised labelling to minimise accidental ingestions. Future prospective research is needed to investigate the reasons behind these therapeutic errors in order to provide targeted prevention strategies.

212. A review of Calls to an Australian Poisons Information Centre from Carers Working in Group Homes

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Objective: To characterise the calls made to the NSW Poisons Information Centre (PIC) from carers looking after people living in a group home (community dwelling for people with disabilities, such as mental illness, intellectual or physical impairment, or low level aged care). *Methods:* A retrospective review of calls made to the PIC in 2008 involving individuals residing in a group home (excluding bites and stings). Only calls from the local state, New South Wales were included. *Results:* Of the 75,467 local calls received by the PIC in 2008, there were 2,044 (2.7%) calls from group homes. The most prominent call type was of medication administration errors (n = 1513; 74%), consisting of - medications missed from previous dose time (36.3%), medications given to wrong client (10.0%), medications given at incorrect time (8.7%), multiple doses of the same medication given in close proximity (8.4%), clients refusing medications (4.4%), seeking advice for clients who will be delayed in receiving medications due to availability issues (4.1%), miscellaneous (2.1%); followed by requests for various types of drug information (13.6%) such as checking drug interactions and generic drug equivalence. Calls occurred throughout the whole day with a bimodal distribution, the major peak in the evening at 5–8 pm followed by a morning peak at 7–10 am. The majority of calls regarding medication errors resulted in advice that the client could remain at home with extra monitoring, with only 31 calls referred immediately to hospital and 8 calls referred immediately to a general practitioner. *Conclusion:* Calls from group homes represent a significant proportion of PIC call volume and require extended time to elicit sufficient history. Many of the enquiries are not appropriate for a poisons information specialist to answer and require the carer to contact the medical practitioner or local pharmacist. Group home facilities require after hours medical and drug information support to provide advice on the management of medication queries, particularly missed and refused medications. As medication errors have the potential for serious adverse effects, better training and procedures are needed for staff working in these facilities to improve medication safety in the community.

213. Medication Errors with Toxic Outcome and Seasonal Variation

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Objective: A descriptive study of the number and nature of medication errors (MEs) leading to drug toxicity in Denmark. *Methods:* All enquiries to Giftlinjen from 2006 (opened in August) to 2009 (9 months) about MEs leading to toxicity were evaluated. *Results:* The number of cases per year was steadily increasing (4 in 2006, 5 in 2007, 18 in 2008 and 26 in 2009) - in total 53 cases. The monthly rate in 2009 was 2.68 new cases. The majority of MEs leading to toxicity took place in June, July and August (3/5 in 2007; 9/18 in 2008; 13/26 in 2009) and in nursing homes in 45% of the cases. There was a higher proportion of antipsychotic drugs or antidepressants involved in these cases (70%) compared to the proportion in the total ME population (34%) or in the total population of enquiries to Giftlinjen (16%). The majority of the cases (26) were categorised "no risk". However, 2 were categorised "temporary effect", 20 "requiring treatment" and 2 "life threatening". The response time i.e. the time from ingestion of the toxin to calling the Poison Centre was 1.1 hrs compared to 2.1 hrs in the remaining cases. *Conclusion:* The number of MEs leading to potentially harmful effects is increasing in Denmark especially in nursing homes during the summer period in which the regular staff members are on leave. The majority of MEs involves antipsychotic or antidepressant drugs, but luckily the majority of incidents are categorised as harmless - this may be due to the rapid enquiry and advice from the Poison Centre. However, we recommend that a special effort be made in nursing homes during the summer period to avoid mixing up medication and to ensure that the correct medication is given to the right patient.

214. Therapeutic Errors Involving Spiriva® (Tiotropium Bromide): Enquiries to UK National Poisons Information Service

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Objective: Spiriva® (tiotropium bromide) is used as a maintenance bronchodilator treatment in chronic obstructive pulmonary disease (COPD). It is available as an inhalation powder in hard capsule form for use in an inhaler (HandiHaler) and also as a solution for inhalation (Respimat). The inhalant capsule is indistinguishable in appearance from oral capsules and can be ingested in error. Enquiries involving tiotropium bromide (Spiriva®) to UK National Poisons Information Service (NPIS) units were reviewed. *Methods:* The number of incidents involving tiotropium bromide reported to UK NPIS units for 18 months from April 2008 to September 2009 inclusive was reviewed. This data was compared with enquiry data regarding all therapeutic errors over the same period. *Results:* 83,215 telephone enquiries relating to patients were received by NPIS, of which 16.9% (14,103/83,215) related to therapeutic errors. Four hundred and sixty-nine enquiries were received regarding tiotropium bromide over this period, of which 467 (99.6%) related to patients. The circumstances involved in the tiotropium enquiries were

as follows: therapeutic errors 456/467 (97.6%); accidental 7/467 (1.5%); intentional 4/467 (0.9%). Where the circumstances were intentional, 3/4 involved additional drugs. One out of four patients was symptomatic (somnolence and abdominal pain) after she deliberately ingested Spiriva® and oxcarbazepine. Of the 456 enquiries regarding therapeutic errors, 448 (98.2%) involved ingestion of a Spiriva® capsule, only 8 (1.8%) enquiries involved inhalation. The total number of enquiries involving Spiriva® ingestion represents 3.2% (448/14,103) of all therapeutic error enquiries received over this period. Eighty-one per cent of tiotropium ingestion patients were aged 60 years and over, compared with 32.9% of all therapeutic error patients. 65.2% of tiotropium ingestion patients were female and 33.7% were male (1.1% unknown). Symptoms were recorded in 8/448 (1.8%) tiotropium ingestion patients. One patient who had ingested 6 Spiriva® capsules developed agitation and urinary retention. *Conclusion:* Enquiries relating to Spiriva® ingestion represent a small proportion of NPIS therapeutic error enquiry workload, however this could perhaps be avoided if the inhalant capsule was easily recognised as such, rather than resembling an oral capsule. The unnecessary administration of a prescribed medication by an ineffective route may result in an exacerbation of (untreated) COPD symptoms. *Acknowledgement:* The authors appreciate the assistance of the other Units of the NPIS in providing data.

215. Paresthesias Following Administration of Intrathecal Chemotherapy Unintentionally Dissolved with 0.9% Benzyl Alcohol

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Objective: Central nervous system prophylaxis of acute lymphocytic leukemia (ALL) involves intrathecal administration of methotrexate or cytarabine. Preservative free diluents are used to limit neurotoxicity. We present a case of transient neurotoxicity from the unintentional dissolution of methotrexate (MTX) and cytarabine with benzyl alcohol. This case describes the consequences of administering a preservative which is normally omitted from intrathecal preparations. *Case report:* A 16 year-old boy with a past medical history of ALL was undergoing prophylactic intrathecal chemotherapy for the past six weeks. The patient presented for his seventh treatment and underwent lumbar puncture without any complications. He received intrathecal MTX 15 mg, cytarabine 50 mg and hydrocortisone 50 mg. During the intrathecal injection, he began to complain of burning pain in both legs. The administration was immediately discontinued. The patient's neurologic examination did not reveal any motor weakness or abnormal rectal tone. The symptoms subsided within five to ten minutes. It was discovered that cytarabine and MTX were unintentionally dissolved in bacteriostatic water which contained 0.9% of benzyl alcohol as a preservative. This was due to a compounding error. The patient was placed in an upright position and interventional radiology was consulted for possible placement of a lumbar drain. He was admitted for observation and did not develop any further neurologic sequelae so no intervention was required. *Conclusion:* Intrathecal chemotherapeutics diluted in solutions containing benzyl alcohol preservative may cause transient paraplegia. The mechanism of neurotoxicity is thought to be due to blockade of nerve conduction. Animal evidence demonstrates reversible nerve conduction blockade when benzyl alcohol is applied to nerve roots without any demyelination. Large doses or chronic exposure to benzyl alcohol typically result in patchy demyelination that is irreversible. Treatment is typically supportive but significant exposures may require aggressive CSF removal and lavage. This case supports the role bacteriostatic preservatives may have in neurotoxicity with intrathecal administration. Caution should be exercised when chemoagents are being prepared.

216. A Case of Near-fatal Flecainide Medication Error in a Neonate

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Objective: Flecainide is an IC antidysrhythmic primarily indicated for ventricular dysrhythmias and supraventricular tachycardia (SVT). Overdose has a reported mortality of 22% and death results from proarrhythmic cardiovascular collapse. Reported cases of flecainide overdose in neonates are rare. We report a near-fatal flecainide overdose in a 15 day-old premature neonate treated for SVT. *Case report:* An 18-day old, 2 week premature, 4-kg boy with normal APGAR scores developed persistently high heart rates (220–240 beats/min) and ECG changes consistent with SVT. There was minimal response to vagal maneuvers, adenosine, and esmolol, and a transthoracic echocardiogram showed no underlying structural abnormality. He was then started on flecainide 4 mg PO Q8h. Following the fourth dose he developed lethargy, cold clammy skin and a heart rate of 40 beats/min with no palpable pulse. Pediatric life support was initiated. Sodium bicarbonate was administered intravenously due to suspected flecainide toxicity. Approximately five minutes after sodium bicarbonate his rhythm converted to a narrow-complex tachycardia. The patient was admitted to the PICU on an epinephrine infusion and mechanical ventilation. The epinephrine infusion was discontinued after approximately twenty-four hours and he was extubated 2–3 days later. The patient showed neurologic improvement and was started on oral timolol with no evidence of SVT and eventually discharged in good health. A serum flecainide concentration was 1360 mcg/L (therapeutic, 200–1000 mcg/L) drawn one hour prior to the cardiac arrest. It was later discovered that a 2-fold dosing error occurred: the patient received 8 mg Q8h instead of 4 mg Q8h for four doses. The flecainide acetate was compounded at the hospital pharmacy and shown to be correct. The error resulted from improper labeling by the pharmacy. *Conclusion:* Other features that make flecainide toxicity challenging to treat are the lack of proven antidotes. The volume of distribution is high, and toxicity rapid, rendering extracorporeal modalities relatively ineffective. Pharmacologic interventions such as amiodarone and lidocaine have been used with success. Experimental evidence and case reports demonstrate that sodium bicarbonate therapy may be the treatment of choice in the setting of flecainide toxicity.

217. Characteristics and Management of Poisoning with Ethylene Glycol and Methanol in the United Kingdom

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Objective: Poisoning with ethylene glycol or methanol is one of the most common reasons for referral to a consultant clinical toxicologist in the UK, because there may be diagnostic difficulty or severe toxicity. In addition, availability of specific assays and antidotes is inconsistent. This retrospective study was performed to describe clinical characteristics and management of ethylene glycol or methanol poisoning to inform future planning of services, including supply of antidotes and assays. *Methods:* Retrospective national study of telephone enquiries to the National Poisons Information Service (NPIS) for the year to September 2008, where the specific terms ethylene glycol or methanol had been used. *Results:* There were 175 NPIS enquiries about ethylene glycol or methanol, involving 148 separate exposures, 24 (16%) of which not systemic. The 124 systemic exposures affected 70 males (56%) and 35 (28%) females (sex not recorded in 19); 112 (90%) involved ethylene glycol, 11 (9%) involved methanol and 1 (1%) involved both. Eight (6%) patients were less than 20 and 12 (10%) more than 50 years old; 39 (31%) cases were recorded as acidotic (pH < 7.3 or "acidotic") and 31 (25%) as admitted to HDU or ITU. Ethylene glycol or methanol concentrations were recorded as performed in 48 cases (39%). Results were <200 mg/L in 7 (14%), 200–500 mg/L in 5 (10%), 500–1000 mg/L in 10 (21%), >1000 mg/L in 10 (21%) and were not available at the time of the enquiry in the remainder (33%). Fomepizole was used in 5 (4%) cases, ethanol in 61 (49%) cases and both in 6 (5%) cases. Dialysis was used or was advised in 33 (27%) cases. *Conclusion:* This preliminary study does not measure incidence of ethylene glycol or methanol poisoning because the search terms do not capture all products containing these substances and because some cases may never be discussed with NPIS. However, it does demonstrate that males are more frequently involved, exposures more commonly involve ethylene glycol and ethanol was the antidote most frequently employed. Further prospective studies are required to estimate incidence and need for assays and antidotes more accurately.

218. Toxicokinetics of Ethanol and Methanol in a Severe Case of Methanol Poisoning

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Objective: Methanol poisoning is a rare event in Spanish EDs. One of its potential causes is a "Universal solvent" widely used in households. The current antidotes for methanol poisoning are ethanol and methylpyrazole, both of them acting as blockers of ADH, preventing the production of toxic metabolites. We present a case showing the difficulties of using ethanol due to its high rate of metabolism. *Case report:* A 45-year old man was found unresponsive at home. He was previously healthy without a previous record of alcohol abuse or psychiatric illness, but under family and professional stress during the previous months. Several cans of chemicals ("Universal solvent", "Zotal" and glue) were found around him. The "Universal solvent" contained methanol and toluene, according to the can, but the concentration was not indicated. The "Zotal", which is used as an industrial disinfectant, contained 0.8% 4-chloro-3-methyl-phenol, 0.4% 4-chloro-2-benzylphenol, and 1.5% 2-phenyl-phenol. He presented in a coma with a Glasgow Scale Score of 3, edema, and burning in his airways. He was admitted to the ICU and supported on mechanical ventilation. Biochemistry and toxicological analysis showed severe metabolic acidosis (pH 6.9, CO_3H 16.7 mmmol/L, and lactate 2.2 mmol/L) and blood methanol concentration equal to 2.27 g/L. Fibrogastroscopy showed Degree II Zargar caustic oesophagitis and gastritis. Acidosis was successfully corrected with sodium bicarbonate. Ethanol perfusion was placed with a loading dose of 1.14 mL/kg in 15 minutes followed by a perfusion of 0.1 mL/kg/h, in accord with our current procedures for non-alcoholic patients. GC/FID analysis for ethanol and methanol was performed once every six hours. The analytical follow-up demonstrated that the ethanol perfusion rate was unable to maintain the required therapeutic concentration (1–1.5 g/L). His blood methanol concentration followed a sloping trend down to zero at 150 hours after poisoning, speeded by one session of hemodialysis. The patient progressed to full recovery without optical, neurological or digestive sequelae and was discharged 1 month after admission. The estimated dose of methanol ingested, assuming a peak concentration of 2.27 g/L and a distribution volume of 0.68 L/kg, was 123.5 g.

219. Ethylene Glycol Poisoning in Children - Therapeutic Aspects

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Objective: The purpose of this study was to describe the prevention, management and clinical course of toxic alcohol ingestions. *Methods:* Data were collected on all patients treated for toxic alcohol ingestions over a

period of 5 years. *Results:* Eleven patients, 5 boys and 6 girls, ages between 2 and 18 years old, presenting toxic ingestions were identified between January 1st 2004 and December 31st 2008. The majority of patients with toxic alcohol exposure were admitted to an intensive care unit and received emergency haemodialysis (9 patients out of 11). All patients presented severe acidosis and, in two cases, severe kidney failure was noted. None of the patients received specific treatment. For 7 patients haemodialysis was indicated for removal of toxin. Besides haemodialysis, the treatment also included support for vital functions, activated charcoal administration and sodium bicarbonate solution to reverse severe acidosis. For seven (7) out of eleven (11) patients the evolution was unfavorable leading to death within 48 hours from admission. *Conclusion:* In absence of specific treatment, sustaining treatment for vital functions and haemodialysis are efficient therapeutic measures in ethylene glycol intoxication. *References:* 1. Megarbane B, Borron SW, Baud F. Ethylene Glycol. In: Shannon M, Borron S, Burns M, eds. Haddad and Winchester's Clinical Management of Poisoning and Drug Overdosage, 4th ed. Philadelphia, USA: Saunders Elsevier Inc. 2007:611–21.

220. Significance of the Osmolal Gap in Suspected Ethylene Glycol Poisoning

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Objective: Ethylene glycol is an uncommon cause of poisoning, for example accounting for only 0.03% of enquiries to the American Association of Poisons Control Centers in 2007.[1] Poisoning severity depends on the extent of exposure but direct laboratory determination is not always immediately available. The 'osmolal gap' is widely relied on as a surrogate marker of the presence of toxic alcohol. The present study sought to examine the utility of the osmolal gap in patients with suspected ethylene glycol poisoning. *Methods:* This was a retrospective analysis of serum ethylene glycol concentrations and matching osmolality determinations between 2004–2008 at the Royal Infirmary of Edinburgh. Osmolality was estimated by [Na+]x2 + [K+] + [urea] + [glucose], and the osmolal gap was calculated from the measured osmolality minus estimated osmolality. Prediction of the presence of ethylene glycol examined by a receiver operating characteristic (ROC). *Results:* There were 87 ethylene glycol determinations (detected in 30, 34%). Osmolality was available in 21 cases, and these were used in the data analysis (ethylene glycol detected in 10, 48%). Osmolal gap was 16 mOsm/L (IQR 5 to 22 mOsm/L) in the absence of ethylene glycol versus 39 mOsm/L (IQR 14 to 45 mOsm/L) in its presence ($p = 0.115$ by Mann Whitney test). ROC found AUC 70.9% (95% CI 47.3 to 88.3%), $p = 0.0715$. The strongest predictor for ethylene glycol was osmolal gap >27 mOsm/L, which gave sensitivity 60% (26 to 88%) and specificity 91% (59 to 99%), positive predictive value 7 (4 to 11), and negative predictive value 0.4 (0.1 to 3). *Conclusion:* The osmolal gap was a poor marker for the presence or absence of ethylene glycol in this group. Further work is required to define the role of serum osmolality measurements in the setting of suspected ethylene glycol poisoning. *References:* 1. Bronstein AC, Spyker DA, Cantilena LR, et al. 2007 Annual Report of the American Association of Poison Control Centers. Clin Toxicol 2008; 46:927–1057.

221. Acute Methylated Spirit Poisoning: The Moroccan Poison Control Centre Experience

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Objective: The present retrospective study aimed to describe the epidemiological, clinical features and outcome of all cases related to methylated spirit poisoning received by telephone or by intoxication reporting form from hospitals sent to the Moroccan Poison Control Centre (MPCC) between January 1992 and December 2007. *Methods:* The demographic features, circumstances, symptomatology, therapeutic aspects and outcome were analyzed. The patient's clinical state was classified according to the Poisoning Severity Score "PSS"[1] and IPCS age groups were used. *Results:* The collected cases (173) represented 50.2% of all cases of alcohol poisonings at the same period. The mean age was 25.96±12.12 years; range from 1 to 70 years. The sex ratio (male/ female) was 5.4 in favour of male. Oral route was involved in 79.1% of the cases and domestic use represented 76.2%. The results also showed that 86.6% of the cases were accidental exposures and 11.5% were related to addiction. The symptomatology was dominated by gastrointestinal and neurological signs. According to PSS, patients presented with moderate signs (grade 2) in 45.2% of cases or severe (grade 3) in 6.2%. The management delay after intoxication was ≤ 4 hours in 78% of the cases. Mortality was 9.5% and sequelae were observed in 5.20%, represented by ophthalmic sequelae. Univariate analysis was conducted to identify factors associated with severe poisoning (grade 3) and death. *Conclusion:* It could be concluded that methylated spirit poisoning is frequent and severe. Patients and health professionals should be aware of the potential danger of such poisoning in order to prevent or limit the consequences. *References:* 1. Persson HE, Sjöberg GK, Haines JA, et al. Poisoning Severity Score. Grading of Acute Poisoning. Clin Toxicol 1998; 36:205–13.

222. The Combination Ethanol-Medicines, A New Entity in Acute Poisoning in Children

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Objective: To study acute intentional medicines and ethanol poisoned patients admitted to a pediatric poisoning department. *Methods:* We have performed a retrospective study of both acute intentional ethanol poisoning and medicines and ethanol poisoning admitted to our department between November 1st 2004 and October 31st 2009. The following criteria were taken into consideration: type of medicine, age, gender, severity of poisoning, hospitalization duration. *Results:* 334 patients with acute intentional poisoning with ethanol alone or in combination were registered during the above mentioned period. Twenty-three patients out of the total of 334 had taken the combination medicine-ethanol. The following medicines were identified using the history and toxicological analyzes: barbiturates 6 cases, benzodiazepines 4 cases, dextromethorphan 3 cases, paracetamol 2 cases, disulfiram 1 case, cannabinoids (marijuana) 1 case, carbamazepine 1 case, metronidazole 1 case, rifampicin 1 case, nifedipine 1 case, doxepin 1 case, dextromethorphan and diazepam 1 case. The median age was 13.5 years. In all cases Poisoning Severity Score was 2 or 3. The combination of ethanol with disulfiram, carbamazepine and dextromethorphan caused the most severe cases. The median length of hospitalization was 2.4 days compared to one in acute intentional ethanol poisoning. Benzodiazepines, barbiturates, marijuana, dextromethorphan were combined with ethanol as recreational drugs; in other situations the ethanol was used to potentiate the action of medicine in suicidal attempts. *Conclusion:* The use of medicines in combination with ethanol in acute poisoning has become a reality in recent years. These combinations are used as recreational drugs or in suicidal attempts. The combination of ethanol with medicines increases the severity of poisoning and consequently the length of hospitalization. *References:* 1. Kuffner EK. Disulfiram and disulfiramide reactions. In: Flomenbaum NE, Goldfrank LR, Hoffman RS, et al, eds. Goldfrank's Toxicologic Emergencies. 8th ed. New York, USA: McGraw-Hill, 2006:1176–81. 2. Kleinschmidt KC. Ethanol. In: Shannon M, Borron S, Burns M, eds. Haddad and Winchester's Clinical Management of Poisoning and Drug Overdose. 4th ed. Philadelphia, USA: Saunders Elsevier Inc. 2007:589–602.

223. Prevalence and Correlation of Levamisole-Adulterated Cocaine and Severe Agranulocytosis/Vasculitis

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Objective: In September 2009, the US Substance Abuse and Mental Health Services Administration issued a release alerting health authorities that cocaine may be adulterated with levamisole, a veterinary anthelmintic. Subsequently, four atypical cases of agranulocytosis, severe cutaneous necrosis and/or vasculitis in cocaine users were observed at our institution in October 2009. The objective of this study was to develop a liquid-chromatography tandem mass spectrometry (LC-MS/MS) method for the detection of levamisole in these cases and to determine the prevalence of levamisole in cocaine positive patient samples. *Methods:* A LC-MS/MS method was developed and validated for the determination of levamisole in urine and plasma samples. Levamisole and an internal standard were monitored in multiple reaction monitoring-information dependent acquisition-enhanced product ion (MRM-IDA-EPI) mode (Applied Biosystems 3200QTRAP®MS/MS). All cocaine-positive urine drug screens, tested in the San Francisco General Hospital Clinical Laboratory in October 2009, were tested for levamisole. LC Time-of-Flight Mass Spectrometry was used for the detection of other cocaine cutting agents, levamisole metabolites and impurities using accurate mass measurements and database searching. *Results:* Out of 970 total urine drug screens, 20.5% were positive for benzoylecgonine (cocaine metabolite) and of those 87% were positive for levamisole. The urines from the four cases of agranulocytosis, severe cutaneous necrosis and/or vasculitis tested positive for levamisole. These cases were characterized by severe cutaneous necrotic lesions localized to the ears and lower extremities, mild to severe neutropenia and infectious complications. Other findings in some but not all of these cases included vasculitis, circulating pANCA, anti-nuclear antibodies, anti-cardiolipin antibodies, increased levels of beta-2-glycoprotein I and abnormal clotting tests. LC-TOF analysis allowed for the differential detection of levamisole metabolites and impurities in the levamisole positive urine samples. Correlation studies are underway to determine if there is a metabolite pattern predictive of an adverse reaction to levamisole-adulterated cocaine. *Conclusion:* The high prevalence of levamisole-adulterated cocaine and resulting toxicity in cocaine users is a serious public health issue. Clinicians should consider the possibility of levamisole-adulterated cocaine in users with unexplained atypical symptoms. Further studies are underway to determine factors which may predispose individuals to levamisole-related neutropenia and/or vasculitis.

224. Increasing Abuse of New Cathinone Derivatives in Sweden - A Poisons Centre Study for the Years 2008–2009

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Objective: Cathinone derivatives, such as mephedrone, MDPV, methedrone, butylone and methylone are sold over the Internet as recreational drugs. These substances bear pharmacological and structural similarity to both MDMA and amphetamine, clinical effects are assumed to be similar. Inquiries to the Swedish Poisons Centre concerning cathinone derivatives have increased rapidly and since few toxicological data are available, all cases were investigated in detail. *Methods:* All inquiries to the telephone service for the years 2008–2009 concerning cathinone derivatives were registered. Fifty two hospital case records were also available. Collected data included type of compound, age, sex, dose, route of exposure, coingestants, geographic location, inquirer,

and clinical features. An evaluation according to the poisoning severity score (PSS) was made in 83 cases where sufficient information was extractable. *Results:* A total of 150 cases were found. All concerned young people (14–38 years old), males being over-represented (71%). Mephedrone was by far the most commonly occurring substance (100 cases), followed by MDPV (25 cases). A lesser number was related to butylone (9 cases), methedrone (6 cases) and methylone (4 cases). The most common route of exposure was oral (54%), followed by nasal insufflation (20%) and intravenous (7%). Clinical symptoms recorded were tachycardia (53%), restlessness (33%), mydriasis (25%), hypertension (14%) and anxiety (14%). Fifty-four per cent of the patients were classified as PSS1 and 22% as PSS2. No severe (PSS3) cases were registered, but there was one with lethal outcome that related to the intake of mephedrone, the only drug present in the blood on post-mortem examination. This previously healthy young woman developed respiratory and circulatory arrest. On arrival at hospital, hyponatraemia (120 mmol/L) and global cerebral oedema were evident. *Conclusion:* Most cases involving cathinone derivatives are benign, but occasional serious effects and even deaths cannot be ruled out. Recently two lethal cases related exclusively to methedrone were reported by the National Laboratory of Forensic Medicine. Mephedrone was classified as a narcotic drug in May 2009. Interestingly, during 2009 it has partly been replaced by the other increasingly popular cathinone derivatives.

225. Viperfav® and Viper Envenomings: A Retrospective Case Review Study

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Viperfav® contains purified F(ab')2 fragments of equine antibodies; one vial can neutralize 500 to 1000 mouse LD50 of European viper venoms and is known to be safe and effective.[1,2] *Objective:* To compare the efficacy of Viperfav® as a function of the delay prior to infusion, and to assess treatments such as antibiotics, corticosteroids and low molecular weight heparin (LMWH). *Methods:* A retrospective study (1999 to 2008) of moderate or severe viper envenomings treated with Viperfav® and collated by the Poisons Centre (PC).[1] The assessment criteria were: duration of hospital stay, complications (hematoma, infection) and persistent functional impairment at day 15. Statistical studies were based on multivariate model (logistic regression). *Results:* 214 moderate and 54 severe envenomings were included. The timing of Viperfav® infusions <10 hours after bites (179 patients vs. 72) significantly reduced the incidence of hematomas (OR 0.43; $p<0.006$) and functional impairment (OR 0.27; $p<10–4$) and the length of hospital stay (OR 0.47; $p<0.03$). Multiple doses of Viperfav® (≥2 vials in 22 patients vs. 246) did not improve the outcome of these assessment criteria. The routine use of antibiotics was prescribed in 102 patients (vs. 166 patients without) and no significant difference was observed regarding the assessment criteria. No infections were recorded in the group receiving no antibiotics. Corticosteroids were prescribed in 36 patients (vs. 232 without) and did not significantly improve the selected criteria or edema. LMWH in 32 patients (vs. 236 without) significantly increased the incidence of persistent functional impairment (OR 3.71; $p<0.003$) and the length of hospital stay (OR 3.21; $p<0.009$). *Conclusion:* Viperfav® is most effective when given early (<10 hours) after envenoming and one vial was effective whatever the grade of envenomation. The routine use of antibiotics, corticosteroids is not necessary and we recommend that LMWH should not be used. *References:* 1. Harry P, De Haro L, Asfar P, et al. Assessment of intravenous immunotherapy with purified F(ab')2 fragments (Viperfav®). La Presse Médicale 1999; 28:1929–34. 2. De Haro L, Lang J, Bedry R, et al. Envenimations par vipères européennes. Etude multicentrique de tolérance du Viperfav®, nouvel antivenin par voie intraveineuse. Ann Fr Anesth Réanim 1998; 17:681–7.

226. Genetic Abnormalities and Delayed Cell Death Observed in Acute Carbon Monoxide Poisoning

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Objective: Carbon monoxide (CO) poisoning remains in Poland a significant health problem, while causes of delayed sequelae are still not completely understood. The aim of the current investigation was to evaluate the mechanism of the delayed cell death and manifestation of the DNA damage in the cultured lymphocytes obtained from blood of patients accidentally exposed to toxic concentrations of CO. *Methods:* The examined group consisted of 74 patients treated at the Department of Clinical Toxicology Jagiellonian University Medical College. Poisoning severity was estimated on basis of neurological symptoms (according to Pach scale), age, duration of exposure, COHb level and blood lactate concentration on admission. The method of Fenech et al[1] was used to obtain material for micronuclei analysis (CBMN) in binucleated cells (BNC) and to estimate percentage of necrotic and apoptotic cells *in vitro*. Nuclear division (NDI) was calculated to determine the proliferation rate. Control samples from healthy donors were analyzed in parallel with the test samples. *Results:* The patients exposed to CO demonstrated significantly higher results of the CBMN assay and frequency of apoptotic cells comparing to the control. Mean values of MN in examined group resulted in 6.58/1000BNC vs 3.41/1000BNC in control, while NDI did not statistically differ in both groups (1.16 vs 1.164). The frequency of MN and NDI depended on the estimated poisoning severity ($p<0.05$). Micronuclei occurrence showed the strongest correlation with age ($\beta = 0.2275$, $p = 0.0024$) and lactate concentration ($\beta = 0.1781$, $p = 0.0230$). The connection between the frequency of MN and apoptotic cells was not observed. *Conclusion:* Obtained data support the thesis about the genotoxic potential of CO, resulting from poisoning severity. Increased frequency of apoptotic and necrotic cells *in vitro* points to the elimination of the *in vivo* injured cells. No correlation between DNA damage (MN) and cell death suggests that the cells with sublethal level of damages do not lose the proliferation potential. Observed abnormalities in genetic material and elevation of NDI in more severe cases may confirm the occurrence of the apoptosis resistant cell clones, which could lead to delayed sequelae and cancer transformation after CO acute poisoning. *Reference:* 1. Fenech M, Crott J, Turner J, Brown S. Necrosis, apoptosis, cytostatis and DNA damage in human lymphocytes measured simultaneously within the cytokinesis-block micronucleus assay: description of the method and the results for hydrogen peroxide. Mutagenesis. 1999; 14:605–612.

227. Managing Opiate Withdrawal: The Clinical Pharmacologist's View

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Objective: To explain the physical features of opioid withdrawal and suggest how they may be managed. *Methods:* The symptoms are categorized and remedies are suggested. *Discussion:* There are two aspects to opiate dependence. 1. The physical effects of opioid withdrawal in the face of mu-receptor down-regulation. 2. The long-lasting problems of neuronal changes in the reward pathway. The physical symptoms of opioid withdrawal are reflected in some of the parameters of the objective opiate withdrawal scale (OOWS): yawning; rhinorrhoea; piloerection; perspiration; lacrimation; tremor; mydriasis; hot and cold flushes; shivering/huddling for warmth; restlessness; frequent shifts of position; vomiting; muscle twitches; and abdominal cramps. Put into groups, the symptoms are of an influenza-like illness, with sore muscles; diarrhoea; restlessness; and too much adrenaline. Simple remedies suffice to make the patient more comfortable: paracetamol or non-steroidal anti-inflammatory drugs; non-absorbable opioids (loperamide); (short-acting) z-drugs such as zopiclone; and alpha-2 agonists (clonidine, lofexidine) or beta-antagonists. The craving, which is associated with changes in the dopaminergic reward pathway, is much more difficult to treat than the relatively brief symptoms of acute withdrawal. Several neurotransmitter systems, including the dopaminergic, cholinergic, noradrenergic, and glutamatergic pathways play a role in psychological dependence. The mu-receptor has a primary role, and knock-out mice that have no mu-receptor are not susceptible to opioid dependence. *Conclusion:* The physical symptoms of opioid withdrawal are treatable, and rarely serious. Strategies to reduce craving can be psycho-social, or pharmacological, and the latter can be opioid agonist, opioid antagonist, or non-opioid.

228. Neonatal Withdrawal Syndromes

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Objective: To delineate the opioid and non-opioid etiologies of neonatal withdrawal syndromes (NWS); to describe the clinical features of NWS, specifically, the neonatal abstinence syndrome (NAS) due to opioids; to describe a scoring system for evaluating and monitoring treatment for neonates exhibiting drug withdrawal; and to review the current scientific evidence for pharmacologic management of withdrawal in opioid-exposed neonates. *Methods:* Scientific literature review and Cochrane database review of neonatal withdrawal syndromes and their treatment. *Results:* Neonatal withdrawal syndromes have been described secondary to maternal use of opioid and non-opioid drugs and other substances during pregnancy. Opioid etiologies include methadone, heroin, buprenorphine, fentanyl, and oxycodone. Non-opioid etiologies of NWS have been described secondary to alcohol, barbiturates, benzodiazepines, marijuana, nicotine, amphetamines, cocaine, and the selective serotonin reuptake inhibitors (SSRIs)[1]; however, it is debatable whether some of these latter substances actually cause a clinical abstinence syndrome or whether the symptoms are a drug intoxication effect. It is estimated that NAS occurs in 55% to 94% of infants born to substance-dependent women. Defining clinical signs and symptoms of a "pure" NWS due to a single agent is difficult as many newborns are actually exposed to poly-substances during gestation. The contributory effect of other substances, including alcohol and nicotine, to the physiologic and behavioral dysregulation after birth must be considered. Presenting symptoms of the neonatal abstinence syndrome (NAS) due to maternal opioid use usually occur within the first 48–72 hours after birth, but may present up to 2–4 weeks of age due to methadone. Severity of NWS depends on the specific drugs/substances, timing, and the frequency of use by the mother during pregnancy. Clinical features of NAS include neurologic hyperexcitability (insomnia, irritability, cry, hypertonia, hyperreflexia, tremors, poor sleep, and convulsions), enteric symptoms (vomiting, diarrhea, feeding disturbances), and sympathetic/parasympathetic dysregulation (sweating, yawning, fever, tachypnea, and congestion/sneezing). The differential diagnosis of NAS includes neonatal sepsis, meningitis, hypoglycemia, and hypocalcemia, and must always be considered in the evaluation. The Finnegan Neonatal Abstinence Scoring System (or adaptations thereof) is one of the most frequently used scales to quantify objectively the severity of the NAS and to guide treatment/response to treatment, although it has never been scientifically validated.[2] Infants are scored on 31 items (as noted above along with failure-to-thrive and skin excoriations) at regular intervals. Treatment for NAS has included pharmacologic (opioids, benzodiazepines, barbiturates, and phenothiazines) and non-pharmacologic interventions. Literature has demonstrated wide variation in practices and inconsistencies in treatment for NWS both in the United States and the United Kingdom/Ireland.[3] Non-pharmacologic therapy is imperative for all infants exhibiting NWS and includes swaddling, slow rocking, environmental controls (low lighting,

"white noise"), and pacifiers. Institution of pharmacologic therapy is necessary in a subset of neonates who are exhibiting excessive symptoms to prevent morbidity (score ≥8). The goal of medication therapy is stabilization of more severely symptomatic infants, allowing them to eat, sleep, gain weight, and interact with caregivers, and then a gradual reduction or weaning of medication to allow hospital discharge. Medication regimens used to treat opioid-induced NAS are variable and institution-dependent, although opioid agonists, primarily methadone and morphine, appear to be most frequently used.[4] Opioid agonist medications are thought to be the most effective agents in the treatment of neonatal neurobehavioral problems related to *in utero* opioid exposure; however, a Cochrane review failed to identify a specific opioid as optimal treatment for infants undergoing opioid withdrawal.[5] Sedatives, such as diazepam, have not been shown to be effective treatment for NWS. Evidence has demonstrated that a combination treatment of opioids and phenobarbital significantly decreases hospital stay and decreases withdrawal severity.[5] Comprehensive reviews of pharmacologic management of NAS have concluded that strong evidence is lacking on the relative efficacy of different medication regimens. Buprenorphine has been found to be a novel, safe and effective treatment for NAS.[6] Clonidine has also been demonstrated to be both safe and efficacious both as single and as an adjunctive therapy to opioids.[7] Polydrug withdrawal is primarily treated with opioids alone and in combination with phenobarbital. Many clinicians advocate that treatment of infants with NWS should be based on symptoms, rather than weight-based dosing, at defined intervals, although this issue has never been studied. Neonatal withdrawal due to maternal use of SSRIs has only recently been described and investigated.[8] Overlap between symptoms caused by drug SSRI drug withdrawal or direct serotonin effects likely exists, although NWS has been demonstrated in symptomatic infants with very low or undetectable levels of drug or active metabolite. Symptomatic treatment and/or phenobarbital for those infants with convulsions have been suggested. Conclusive evidence for a "true" neonatal cocaine abstinence syndrome is equivocal, as cocaine and its metabolites have been found in neonatal urine for as long as 7 days postdelivery. *Conclusion:* The use of opioid agonists (morphine and buprenorphine) and clonidine as adjunct therapy are needed for infants with severe withdrawal symptoms due to passive maternal exposure of opioids. Additional research is needed to provide more optimal and standardized methods for evaluation and treatment of NWS. *References:* 1. Wang M. Perinatal drug abuse and neonatal drug withdrawal. eMedicine Pediatrics: Neonatology; http://emedicine.medscape.com/article/978492; accessed 11/15/09. 2. Finnegan L, Connaughton J, Kron R, et al. Neonatal abstinence syndrome: assessment and management. Addict Dis 1975; 2:141–58. 3. O'Grady MJ, Hopewell J, White MJ. Management of neonatal abstinence syndrome: a national survey and review of practice. Arch Dis Child Fetal Neonatal Ed 2009; 94:F249–52. 4. Jansson LM, Velez M, Harrow C. The Opioid exposed newborn: assessment and pharmacologic management. J Opioid Manag 2009; 5:47–55. 5. Osborn DA, Jeffery HE, Cole MJ. Opiate treatment for opiate withdrawal in newborn infants (Review). Cochrane Database Sys Rev 2005; 3:CD002059. 6. Kraft WK, Gibson E, Dysart K, et al. Sublingual buprenorphine for treatment of neonatal abstinence syndrome: a randomized trial. Pediatrics 2008; 122:e601–7. 7. Agthe A, Kim GR, Mathias KB, et al. Clonidine as an adjunct therapy to opioids for neonatal abstinence syndrome: a randomized controlled trial. Pediatrics 2009; 123:e849–56. 8. Klinger G, Merlob P. Selective serotonin reuptake inhibitor induced neonatal abstinence syndrome. Isr J Psychiatry Relat Sci 2008; 45:107–13.

229. Naloxone is Overused in the Prehospital Setting

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Objective: Many clinicians would argue that the only appropriate use of naloxone in the prehospital setting is to improve a patient's ventilatory status, and administering it inappropriately could cause harm to patients and prehospital providers. We sought to determine what percent of naloxone administrations are for hypoventilation, and of these, how accurate providers are in predicting who will respond. *Methods:* Setting: a large, suburban Emergency Medical Services (EMS) system with approximately 20,000 Advanced Life Support (ALS) requests per year. Design: Retrospective cohort study. Population: Consecutive patients treated prehospitally with naloxone over an 18 month period. Vital signs on initial ALS evaluation and on arrival in at the Emergency Department (ED) were recorded. *A priori*, hypoventilation was defined as an initial respiratory rate (RR) <9 or a pulse oximetry <92%. Patients defined as having a positive response to naloxone were not intubated and had an increase of 4 or more breaths per minute or an increase in pulse oximetry of 8%. Percentages and 95% confidence intervals (CI) were calculated. *Results:* Of 41,804 ALS requests, 324 (0.8%) patients were treated with naloxone. 54% were male and the average age was 51 years. Of these patients, 102 (31% (CI: 26–37%) were hypoventilating at the time of initial paramedic evaluation. Among the hypoventilating patients, 53 patients (52% (CI: 42–62%) had a positive response to the naloxone and 39 patients (38% (CI: 29–48%) needed to be intubated despite treatment. *Conclusion:* Two-thirds of patients our ALS providers treat with naloxone are not hypoventilating, suggesting that it is being administered for other reasons. This overuse could result in harm to patients and providers. When used in patients that are hypoventilating, one-half improve without the need for invasive airways. Naloxone use should be limited to hypoventilating patients, where frequently effective and unlikely to cause harm.

230. Benzodiazepine Withdrawal

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Objective: The main objective of this presentation is to review the most recent research regarding benzodiazepine withdrawal, particularly emphasizing the cellular mechanisms of tolerance and withdrawal. A secondary objective is to use the information obtained to develop a literature-based management strategy for patients who develop consequential benzodiazepine withdrawal syndromes. *Methods:* A comprehensive search of the medical literature was performed using the key words: benzodiazepine, tolerance, withdrawal. Pertinent articles were reviewed and their references were hand searched for additional information. Levels of evidence were graded using standardized methodology. *Results:* In stark contrast to the wealth of information discussing ethanol and opioid withdrawal, surprisingly little is written on benzodiazepine withdrawal. Specifically, there are no large case series of patients with benzodiazepine withdrawal. In addition, although some medication trials exist, there are no randomized controlled trials of therapy in patients with moderate to severe benzodiazepine withdrawal syndromes. Current pharmacologic interventions were evaluated in a recent Cochrane review, which concluded that larger trials are required.[1] As a result, the majority of the discussion will focus on animal models of benzodiazepine withdrawal with analogies made to humans, when they appear to be physiologically acceptable. Unlike ethanol, there is no evidence of metabolic tolerance to benzodiazepines and therefore tolerance is felt to be mediated by receptor plasticity. In isolated cell preparations, chronic benzodiazepine administration results in impaired GABAergic transmission when benzodiazepines are present, and augmented transmission for a short period of time following removal of benzodiazepines.[2] Similar to chronic ethanol administration chronic benzodiazepine administration appears to shift the populations of GABA subunits such that there is a decrease in alpha-1, alpha-2 and gamma-2 subunits, and a concomitant increase in alpha-4 and gamma-3 subunits.[3–5] While these combined effects would confer an insensitivity to benzodiazepine binding, the lack of widespread distribution of these changes casts doubt as to whether GABA receptor effects are sufficient to account for benzodiazepine tolerance. AMPA (alpha-amino-3-hydroxy-5-methyl-4-isoxazole proprionic acid) receptors, one of the ionotropic glutamate receptor types, are highly localized in specific areas of the brain in concert with NMDA receptors. Since glutaminergic pyramidal cells and GABAergic chandelier cells often lie in close proximity, investigations have evaluated the role of excitatory amino acids in benzodiazepine tolerance and withdrawal. Rat brain slices demonstrate a significant increase in AMPA receptor function during benzodiazepine withdrawal which appears to be mediated through expression of glutamate-R1 receptors.[6] Similarly, AMPA-receptor deficient mice have reduced benzodiazepine tolerance and increased flumazenil-precipitated withdrawal.[7] Clinical withdrawal in animals and humans resembles alcohol withdrawal with a predominance of anxiety and autonomic findings. Although it is generally felt that benzodiazepine withdrawal is comparatively mild, this perception cannot be substantiated and cases of seizures, delirium and death are described. *Conclusion:* Animal models suggest a parallel between ethanol and benzodiazepine withdrawal that includes a loss of GABAergic tone (impaired inhibition) combined with enhanced glutaminergic tone (enhanced excitation). In mild cases carbamazepine, oxcarbazepine or tiagabine may have utility but required more detailed interventions and are largely unstudied in moderate to severe withdrawal.[1] For most patients, therapy with benzodiazepines seems a reasonable first gesture, substituting long-acting therapy (drugs with active metabolites) for short acting drugs when present. It should be noted that acute benzodiazepine treatment may be ineffective at reversing alterations in excitatory tone. As such, when patients are severely ill, the use of excitatory amino acid antagonists such as propofol should be considered if treatment with benzodiazepines fails. *References:* 1. Denis C, Fatséas M, Lavie E, et al. Pharmacological interventions for benzodiazepine mono-dependence management in outpatient settings. Cochrane Database Syst Rev 2006; 3:CD005194. 2. Zeng XJ, Tietz EI. Benzodiazepine tolerance at GABAergic synapses on hippocampal CA1 pyramidal cells. Synapse 1999; 31:263–77. 3. Brett RR, Pratt JA. Changes in benzodiazepine-GABA receptor coupling in an accumbens-habenula circuit after chronic diazepam treatment. Br J Pharmacol 1995; 116:2375–84. 4. Holt RA, Martin IL, Bateson AN. Chronic diazepam exposure decreases transcription of the rat GABA(A) receptor gamma2-subunit gene. Brain Res Mol Brain Res 1997; 48:164–6. 5. Holt RA, Bateson AN, Martin IL. Chronic treatment with diazepam or abecarnil differently affects the expression of GABAA receptor subunit mRNAs in the rat cortex. Neuropharmacology 1996; 35:1457–63. 6. Song J, Shen G, Greenfield LJ Jr, et al. Benzodiazepine withdrawal-induced glutamatergic plasticity involves up-regulation of GluR1-containing alpha-amino-3-hydroxy-5-methyl-isoxazole-4-propionic acid receptors in Hippocampal CA1 neurons. J Pharmacol Exp Ther 2007; 322:569–81. 7. Aitta-Aho T, Vekovischeva OY, Neuvonen PJ, et al. Reduced benzodiazepine tolerance, but increased flumazenil-precipitated withdrawal in AMPA-receptor GluR-A subunit-deficient mice. Pharmacol Biochem Behav 2009; 92:283–90.

231. Alcohol Withdrawal Syndrome: Mechanisms, Features and Management

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Introduction: The alcohol withdrawal syndrome may develop in patients admitted to hospital for an unrelated illness (e.g. for an operation) or patients may present in a confused state to the Emergency Department due to the onset of the syndrome. In both these circumstances, which are medical emergencies, the diagnosis is often delayed as it is not considered. When considered, treatment is often less than optimal. In the past, the mortality

from alcohol withdrawal was high, often as much as 15%,[1] but with advances in recognition and treatment, a more recent study showed an overall mortality of 2%,[2] although 8% of those who developed delirium in this study died.[2] *Definition and features:* The alcohol withdrawal syndrome follows the abrupt discontinuation of, or at least the rapid decrease in intake of, alcohol after heavy and prolonged use. The syndrome is characterized by autonomic hyperactivity, tremor, anxiety and restlessness and is occasionally complicated by seizures, hallucinations and delirium. The DSM-IV diagnostic criteria for alcohol withdrawal are met when two or more of the following are present: autonomic hyperactivity (e.g. sweating or pulse rate greater than 100 bpm); increased hand tremor; insomnia; psychomotor agitation; anxiety; nausea or vomiting; rarely, grand mal seizures or transient visual, tactile or auditory hallucinations or illusions. *Mechanisms:* The mechanisms underlying the syndrome include a reduced activity of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), enhanced activity of the excitatory transmitter glutamate and reduced dopamine release (3). While alcohol enhances the effect of GABA on GABA-A neuroreceptors, resulting in decreased overall brain excitability, chronic use results in a compensatory decrease of GABA-A neuroreceptor response to GABA, evidenced by increasing tolerance to the effects of alcohol. With the onset of alcohol withdrawal, there is a sudden relative deficiency in GABA neurotransmitter activity, which is believed to contribute to the anxiety, increased psychomotor activity and seizures observed. Conversely, alcohol inhibits glutamate receptors (N-methyl-D-aspartate, NMDA receptors) and chronic alcohol use results in up-regulation of these receptors so that more alcohol is required to achieve receptor inhibition. Abrupt cessation of alcohol results in brain hyperexcitability as glutamate inhibition is removed. Brain hyperexcitability manifests clinically as anxiety, irritability, agitation, tremors and withdrawal seizures. In addition, significant increases in plasma norepinephrine have been found, at least for the first 24 hours after cessation of alcohol with significant down regulation of the $\alpha 2$ receptor, which contribute to the autonomic features. *Management:* Patients will often complain of withdrawal symptoms but have no objective evidence of withdrawal; objective assessment is therefore mandatory. Careful monitoring (hourly in severe cases) using the revised Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) score will ensure that any change in the severity of withdrawal is identified promptly. The scale is simple to use and can be employed not only to quantify the severity of the alcohol withdrawal syndrome but to medicate patients going through withdrawal, particularly if the symptom-triggered approach is adopted. This approach offers several advantages. First, patients with no or only mild symptoms are not obtunded by the routine use of drugs such as benzodiazepines. It is inappropriate to prescribe drugs if only minor features of withdrawal are present. Secondly, the period of detoxification is shorter and, thirdly, alcohol abusers learn how to exercise immediate non-pharmacological control over their life. If drug treatment is required, patients should be treated with regimens that are patient specific and flexible to respond to changes in severity of withdrawal (that is they are symptom triggered). Fixed-schedule regimens, where the patient is given a standard regimen irrespective of their symptoms, are inappropriate. Saitz et al[4] reported the clinical course in 101 inpatients who were randomized to receive either a fixed-schedule regimen (n = 50) or a symptom-triggered regimen (n = 51). A symptom-triggered approach decreased both treatment duration and the amount of benzodiazepine administered. Following a meta-analysis, the American Society of Addiction Medicine produced an evidence-based Practice Guideline and concluded that when the CIWA-Ar score is ≥15 the use of a symptom-triggered regimen reduced the risk of major complications developing.[5] Benzodiazepines are the agents of first choice as they have better documented efficacy. They are more effective than placebo in reducing the signs and symptoms of alcohol withdrawal and in reducing the incidence of seizures and delirium[5,6] and have a greater margin of safety than other drugs. Furthermore, benzodiazepines may be given orally or intravenously and a specific antidote, flumazenil, is available in case of unintentional overdose. There is some evidence that longer-acting benzodiazepines (e.g. diazepam) may be more effective in preventing seizures and may produce a smoother withdrawal course with less break-through or rebound symptoms than shorter-acting agents. All patients should receive thiamine 100 mg b.d. orally, unless Wernicke's encephalopathy or Korsakoff's psychosis is suspected, when parenteral administration of B vitamins is appropriate. *Conclusion:* The CIWA-Ar scale should be used to determine both the severity of withdrawal and the need for treatment. If drug treatment is required, a symptom-triggered regimen should be employed using a benzodiazepine. *References:* 1. Victor M, Adams RD. The effect of alcohol on the nervous system. Res Publ Assoc Res Nerv Ment Dis 1953; 32:526–73. 2. Ferguson JA, Suelzer CJ, Eckert GJ, et al. Risk factors for delirium tremens development. J Gen Intern Med 1996; 11:410–4. 3. Vale A. The management of alcohol withdrawal. Medicine 2006; 34:323–7. 4. Saitz R, Mayo-Smith MF, Roberts MS, et al. Individualized treatment for alcohol withdrawal: randomized double-blind controlled trial. JAMA 1994; 272:519–23. 5. Mayo-Smith MF, Cushman P, Jr, Hill AJ, et al. 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232. Valproate is Associated with Fewer Side Effects and Less Complications During Alcohol withdrawal Therapy Compared to Carbamazepine: Results of a Retrospective Cohort Study

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Objective: Seizures and occurrence of *delirium tremens* are frequent complications during alcohol withdrawal therapy. The adjunctive use of the anticonvulsants carbamazepine (CBZ) or valproic acid (VPA) may prevent these complications. However, it is still under debate whether CBZ or VPA should be the preferred drug. We therefore compared the frequency of complications (e.g. seizures, *delirium tremens*), incidence of adverse drug reactions along with other withdrawal related parameters during therapy with VPA and CBZ in a large retrospective cohort study of alcohol withdrawal patients. *Methods:* Retrospective cohort study of patients treated in our department for alcohol withdrawal therapy during 2002–2009. Comparison of patients treated with CBZ (n = 290; from 2002–2006) or VPA (n = 300; from 2006 until now) with otherwise identical therapy. *Results:* Standardized oral alcohol withdrawal therapy comprised of thiamine and symptom-triggered treatment with clonidine and clomethiazole. Oral CBZ (600–800 mg per day) or VPA (900–1200 mg per day) was initiated simultaneously to clomethiazole therapy. Both groups were comparable regarding age, sex, comorbidity (e.g. liver cirrhosis) and cause of admission (e.g. elective, ethanol intoxicated, manifest withdrawal symptoms). There was no significant difference regarding laboratory parameters, hemodynamics, coingested drugs (e.g. benzodiazepines), dose of clomethiazole and clonidine, severity of withdrawal symptoms or need for additional rescue therapy (e.g. neuroleptics, lorazepam). Necessity for medical treatment (86±47 versus 99±58 hrs) and length of stay (7.8±5 versus 9.3±7 days) was shorter in the VPA group compared to the CBZ group. Need for intensive care treatment (e.g. severest withdrawal signs, *delirium tremens*) was significantly infrequent in the VPA- (1%) versus CBZ-group (10%). Additionally, withdrawal related complications (seizures, occurrence of *delirium tremens*) were significantly rare in the VPA-group (10.7%) compared to the CBZ-group (16.2%). Finally, adverse drug reactions (mainly affecting the CNS) were significantly more frequent in the CBZ-group (10%) compared to the VPA group (2.3%). *Conclusion:* Our data suggests that VPA during withdrawal therapy is associated with fewer side effects, infrequent complications (seizures, delirium) and shorter duration of medical treatment compared to CBZ. These results should be confirmed in a larger, prospective setting.

233. Evaluation of the Cardiovascular Autonomic Nervous System and Myocardium Function in Ethanol Withdrawal and Dependence

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Objective: The aim of the study was to assess the risk factors and state of the cardiovascular autonomic nervous system in ethanol withdrawal and to evaluate the myocardium function in ethanol dependent patients. *Methods:* A standard Ewing battery tests (VariaCardio TF5 system) was used for cardiovascular autonomic nervous system assessment in 85 alcoholics with no history of cardiovascular disease (17 females, 68 males), aged from 27 to 68 years (45.7±8.8) treated for withdrawal syndrome. Rest scintigraphic heart examination (99mTc-MIBI-GSPECT, QGS programme) with myocardial perfusion assessment and heart function quantitative analysis (LVEF, EDV, ESV), wall thickening/motion analysis (WTA/WMA) was performed in 10 ethanol dependent males, aged from 29 to 45 years (37.4±4.9). The changes in myocardial perfusion were graded semiquantitative (0 - normal scan, I° - non homogenic tracer uptake, II° - diminished and small foci of tracer absence, III° - visible diminished uptake of tracer + one bigger "cold spot". *Results:* The mean duration of ethanol dependence was 13.7±8.2 years, the mean blood ethanol concentration on admission in the withdrawal group was 1.07±1.21 g/L. In 92% of examined patients severe and in 8% moderate ethanol withdrawal syndrome was diagnosed. An early parasympathetic damage was stated in 23.5% patients, definite parasympathetic damage in 44.7%, a combined parasympathetic and sympathetic damage was diagnosed in 3.5% of patients. The relative risk for parasympathetic and sympathetic system injury rose together with CIWA-A scoring, blood ethanol concentration on admission (OR = 1.4 95% CI: 0.81 ± 2.4). In the group of ethanol dependent patients (mean time of dependence - 10.7 ± 5.2 years) the abnormalities in myocardial perfusion (GSPECT), especially inferior wall and apical region, were present in all patients (I° - 3, II° - 5, III° - 2 patients). Left ventricle ejection fraction (LVEF) was 42 - 65% (average: 56.75%). Indicators of segmental WTA/WMA calculated by QGS program were significantly lower in seven patients. *Conclusion:* In almost 72% of patients treated for withdrawal syndrome cardiovascular autonomic nervous system abnormalities were described. The 99mTc-MIBI GSPECT examination confirmed significant disturbances in myocardial perfusion and heart function in patient with ethanol dependence.

234. Hallucinogenic Mushrooms: Should they be Forbidden?

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Objective: Hallucinogenic mushrooms are increasingly available. After some serious incidents with tourists who

had used magic mushrooms, the Dutch government asked the "Coordination Centre for Assessment and Monitoring of new Drugs" (CAM) for a risk assessment. *Methods:* The CAM, with experts from scientific institutes involved in monitoring, research, and criminal investigation related to drugs of abuse, performed a risk assessment on hallucinogenic mushrooms according to established procedures: review of available literature, scoring of the risks for individual health, public health, public safety, and organized crime. *Results:* Scientifically, the risk assessment is straightforward: acute toxicity is mainly confined to anxiety or panic attacks and chronic toxicity to the occurrence of flashbacks. The number of incidents reported is low. The risks for disturbing public order and criminal involvement are small. The Amsterdam municipal health department described that in 1 out of 2500 cases of mushroom use, an ambulance was called. Ninety-two per cent of these calls concerned tourists. Only 2 out of 100,000 uses actually led to hospital admission. Tourists are considered a vulnerable group, using magic mushrooms in an unfamiliar setting, sometimes impatiently taking an overdose while waiting for the hallucinogenic effects to occur. The CAM advised the provision of high quality user information especially aimed at tourists.[1] The CAM explicitly warned that prohibiting hallucinogenic mushrooms could create new, more dangerous situations: the use of stronger hallucinating drugs, and possible criminal involvement like hiding psilocybin in chocolates. Nevertheless, the Minister of Health prohibited the selling and use of hallucinogenic mushrooms in 2008. The arguments of the CAM were considered valid, but too difficult to carry out. *Conclusion:* Up till now the NPIC received fewer questions on magic mushroom use, but more on other drugs of abuse like GHB and cocaine. After the prohibition of magic mushrooms in the UK in 2005 its use declined in the first year and remained stable later on. The use of cocaine increased.[2] *References:* 1. Coördinatiepunt Assessment en Monitoring nieuwe drugs. Risicoschatting van psilocine en psilocybine bevattende paddenstoelen (paddos's). Bilthoven 2007. http://www.rivm.nl/bibliotheek/digitaaldepot/cam_paddo_advies.pdf 2. Hoare, J. Drug Misuse Declared: Findings from the 2008/09 British Crime Survey England and Wales. July 2009. http://www.homeoffice.gov.uk/rds/pdfs09/hosb1209.pdf

235. Chronic Digoxin Toxicity, Serum Potassium, and Fab Failure: A Case-control Study

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Objective: In contrast to patients with acute digoxin overdose, the prognostic utility of the serum potassium concentration for patients with chronic digoxin toxicity is unclear. We aimed to evaluate this relationship, since in our practice chronic toxicity is more prevalent than acute digoxin overdose. *Methods:* Study design was retrospective case-control. The setting was a Poison Control Center (PCC) and an urban tertiary referral hospital. Cases were defined as PCC referrals with chronic digoxin toxicity resulting in fatality over a 7-year period (2000–06). Controls were defined as hospitalized patients with PCC referral for chronic digoxin toxicity requiring bedside medical toxicology consultation over a one-year period (2006–07) surviving to hospital discharge. All subjects had digoxin toxicity evidenced by an elevated serum digoxin concentration (SDC), consistent clinical symptoms, abnormal ECG findings, and lack of acute overdose by history. Fab failure was defined as fatality despite administration of an appropriate dose of the antidote. Data for evaluation included demographics, SDC, creatinine, and pre-treatment serum potassium concentration. Computer analysis using SPSS included confidence intervals (CI), t-test (continuous data), Fisher exact test (nominal data), and receiver operating characteristics (ROC). *Results:* During the study period, there were 6 fatalities (cases) and 8 survivors (controls), of whom 5 cases (83%) and 5 controls (63%) received digoxin-specific Fab. Elevated pre-Fab serum potassium was highly associated with fatality (t-test $p < 0.05$). Using a cutoff of 5.0 mEq/L for serum K yielded 100% sensitivity (CI 73–100). The ROC area under the curve was 0.81. There were no statistically significant differences between cases and controls with respect to SDC, creatinine, age, or gender. All 5 Fab failures occurred in patients with the combination of both bradycardia (HR range 22–53) and hyperkalemia (range 5.3–7.5 mEq/L). Limitations of this study include a small number of cases, possible misclassification of chronic toxicity by history, and influence of co-medications on potassium such as diuretics. *Conclusion:* Elevated serum potassium prior to treatment with Fab is associated with fatality in chronic digoxin toxicity. The combination of bradycardia and hyperkalemia predicted Fab failure. Future studies are warranted to confirm these findings.

236. Oxatomide-Induced QTc Interval Prolongation in Pediatric Patients After Single and Repeated Overdose

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Objective. To investigate the ability of oxatomide, predominantly used in paediatric patients in Italy, to affect cardiac repolarisation and to induce QT prolongation. *Methods:* In a retrospective study all cases of paediatric oxatomide overdose referred to Pavia Poison Center over a ten-year period (from January 1999 to December 2008) were analyzed. Circumstances of overdose, symptoms and QTc interval were evaluated for each patient. Serum oxatomide levels were measured using an HPLC method. Lack of information on follow-up for at least 6 hours post overdose was considered an exclusion criterion (193 patients were excluded for this reason). *Results:* 169 patients (mean age 29.3 ± 23.9 months) were included in the study. One hundred and forty patients had ingested a single high dose (group 1), 27 had repeated overdose resulting from regular therapeutic error (group 2); in two patients no data were available. Twenty-nine patients developed QTc prolongation (17.1%): the incidence was significantly higher ($p = 0.02$) among patients of group 2 (9/27, 33.3%, OR 3.18) compared to those of group 1 (19/140, 13.5%). Therapeutic dose of oxatomide is 0.5 mg/kg bid. In group 1 the median ingested dose was 23.4 mg/kg in patients with QTc prolongation (LQT) and 14.4 mg/kg in patients with normal QTc (NQT) ($p = 0.06$). Neurological symptoms (dizziness, drowsiness, extrapyramidal effects, seizures) appeared in 75.9% of patients that manifested LQT (22/29) and 56.4% of NQT patients (79/140) ($p = 0.06$, OR 2.39). Other ECG alterations were present in 20.7% of LQT patients (6/29) and 5.7% of NQT patients (8/140) ($p = 0.02$, OR 4.3). The serum oxatomide level was measured 5 hours after ingestion in 15 patients; the mean levels were 950±760 ng/mL in 9 LQT patients and 593±418 ng/mL in 6 NQT patients. No patients showed dysrhythmias, and in all cases QTc was normal at recovery. *Conclusions:* Overdose of antihistamines has often been associated with prolongation of the QTc interval. However, no data are available on oxatomide in this respect. Our observations indicate that oxatomide poisoning can prolong QTc interval in children, especially after repeated overdose.

237. Assessment of the QT Interval After Antidepressant Overdose

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Objective: Torsade de pointes is a rare complication of drug toxicity. A QT-heart rate nomogram has recently been proposed for risk prediction.[1] This study examined the performance of the nomogram after antidepressant overdose. *Methods:* ECG data were examined retrospectively after antidepressant overdose.[2–4] Ingested doses were expressed as multiples of the defined daily dose; citalopram 20 mg, mirtazapine 30 mg and venlafaxine 100 mg. QTc was calculated by Bazett's formula. *Results:* There were 858 recordings from 541 patients (see Table 1). QT values were above the nomogram in 2.4% (95% CI 1.4 to 4.1%), and more likely to be above the nomogram after citalopram overdose than mirtazapine or venlafaxine (difference 7.0%, 95% CI 2.9 to 11.9%, $p = 0.001$). *Conclusion:* Citalopram is a recognised cause of torsade de pointes whereas venlafaxine and mirtazapine are not. Consistent with this, the nomogram discriminated between agents. The nomogram needs further evaluation in predicting arrhythmia. *References:* 1. Chan A, Isbister GK, Kirkpatrick CM, et al. Drug-induced QT prolongation and torsades de pointes: evaluation of a QT nomogram. QJM 2007; 100:609–15. 2. Waring WS, Good AM, Bateman DN. Lack of significant toxicity after mirtazapine overdose: a five-year review of cases admitted to a regional toxicology unit. Clin Toxicol 2007; 45:45–50. 3. Howell C, Wilson AD, Waring WS. Cardiovascular toxicity due to venlafaxine poisoning in adults: a review of 235 consecutive cases. Br J Clin Pharmacol 2007; 64:192–7. 4. Waring WS, Gray JA, Graham A. Predictive factors for generalized seizures after deliberate citalopram overdose. Br J Clin Pharmacol 2008; 66:861–5.

238. Drugs Associated with Hemorrhagic Pancreatitis in the Food and Drug Administration Adverse Event Database and Mitochondrial Toxicity

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Objective: To identify drugs with a disproportional high postmarketing reporting of hemorrhagic pancreatitis

Table 1. Dose as multiple of the defined daily dose (DDD) as median and interquartile range. QT shown as proportion and 95% confidence interval. P-values are for two-tailed Yates' corrected chi square comparison to the citalopram group

	Citalopram n = 215	Venlafaxine n = 223	Mirtazapine
Ingested dose (DDD)	16 (10–30)	15 (9–28)	15 (8–27)
QTc ≥440 ms	68	41	16
	32% (26–38%)	18% (14–24%)	16% (10–24%)
		P = 0.002	P = 0.004
QTc ≥500 ms	4	2	0
	2% (1–5%)	1% (0–3%)	0% (0–4%)
		P = 0.651	P = 0.392
QT ≥ nomogram	10	3	0
	5% (2–9%)	1% (0–5%)	0% (0–4%)
		P = 0.075	P = 0.060

and evaluate the mechanisms of action that may be involved. *Methods:* The FDA's Adverse Event Reporting System (AERS) was searched for the drugs that had the highest adjusted disproportionality reporting ratio for the preferred MedDRA term, hemorrhagic pancreatitis. We identified these signals by using the Multi-item Gamma Poisson Shrinker (MGPS) statistical algorithm that applies a Bayesian model to simultaneously analyze disproportionality of reporting ratios for each event in the huge AERS database (including hemorrhagic pancreatitis) relative to all other events in the whole database. To help reduce false positives, MGPS systematically "shrinks" unstable observed-expected ratios and adjusts for background differences in relative reporting rates by using stratification. The final score is the Empirical Bayesian Geometric Mean (EGBM) score. We found that the list of drugs generated by the algorithm included drugs known to cause mitochondrial toxicity. A PubMed search was performed on each drug to determine effects on mitochondrial function. *Results:* MGPS generated the following top EBGM scores and number of reports (EGBM, N) for the following drugs: asparaginase (25.1, 16), valproic acid (19.2, 88), stavudine (18.2, 30), pegaspargase (12.5, 5), didanosine (11.2, 19), pentamidine (10.5, 6), fluphenazine (7.1, 7), lamivudine (5.8, 18), efavirenz (5.3, 12), nelfinavir 4.7, 8), prednisolone (4.4, 10), drotrecogin-alpha (4.2, 5), olanzapine (3.9, 20) and fenofibrate (3.7, 5). The drugs inhibit a number of mitochondrial complexes. Impaired mitochondrial complexes included asparaginase (II), valproate (II), stavudine (I, II, IV), fluphenazine (I), furosemide (II, III), prednisolone (IV, V), olanzapine (II) and fenofibrate (I, II, III, IV). Other actions of the drugs included uncoupling of oxidative phosphorylation (pentamidine) and inhibition of electron transport (furosemide, prednisolone). *Conclusion:* Most drugs that are associated with a high adjusted relative postmarketing reporting ratio for hemorrhagic pancreatitis appear to impair mitochondrial function and/or electron transport. Further research into the potential role of mitochondrial toxicity and hemorrhagic pancreatitis appears warranted. Likewise, antidotes such as L-carnitine that improve mitochondrial oxidation may warrant further study. Analysis of the AERS database can be used to generate hypotheses about the mechanisms for drug-induced toxicity.

239. Clinical Effects of Red-bellied Black Snake (*Pseudechis porphyriacus*) Envenoming and Correlation with Venom Concentrations

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Objective: There are few reports of red-bellied black snake (RBBS) envenoming. We investigated the clinical features and laboratory findings in patients with definite RBBS (*Pseudechis porphyriacus*) envenoming, including correlation with venom assays. *Methods:* Patients with definite RBBS bites were included from the Australian Snakebite Project, a prospective multicentre study. Demographics, clinical information, laboratory tests and antivenom treatment are recorded prospectively for the study. Venom concentrations were measured in serum samples using a RBBS-antibody enzyme immunoassay (EIA) with a limit of detection of 0.1 ng/mL. *Results:* There were 71 definite RBBS bites and envenoming occurred in 48 patients (68%). Envenoming was characterised by local pain and swelling in all cases, non-specific systemic effects in 44 patients (92%), anticoagulant coagulopathy with an isolated raised activated partial thromboplastin time in 26 patients (54%) and significant myotoxicity in 3 patients (6%). One patient required intubation for severe myotoxicity resulting in muscle weakness and there were no deaths. Pre-antivenom blood samples were available in 35 of 71 patients, including 29 envenomed cases. Venom was not detected in all 6 non-envenomed patients. The median peak venom concentration in envenomed patients was 19 ng/mL (interquartile range: 14 to 72 ng/mL; range 3 to 325 ng/mL). Higher concentrations were associated with coagulopathy (median: 54 ng/mL; range: 5 to 325 ng/mL) and the venom concentrations in two patients with significant myotoxicity were 88 and 162 ng/mL. The median peak venom concentration in patients given antivenom was 88 ng/mL (range: 17.6 to 325 ng/mL). Eighteen patients received antivenom and thirteen had post-antivenom blood samples tested for venom. In all thirteen no venom was detected post-antivenom, including seven patients given one vial of tiger snake antivenom, two patients given two vials of tiger snake antivenom and two patients given half and one vial of black snake antivenom. *Conclusion:* RBBS envenoming is characterised by non-specific systemic effects, anticoagulant coagulopathy and uncommonly myotoxicity. Venom concentrations appear to correlate well with the severity of envenoming. Both tiger snake and black snake antivenoms bind all venom and one vial of tiger snake antivenom appears to be the most appropriate treatment.

240. A Controlled Clinical Trial of a Novel Antivenom in Patients Envenomed by *Bungarus multicinctus*

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Objective: In northern Vietnam, a majority of severely envenomed patients are bitten by *Bungarus multicinctus* (Chinese krait, many-banded krait). Hitherto, these victims have received supportive care only. The aims of this study were to assess the possible efficacy and side effects of a new antivenom. *Methods:* This controlled clinical trial was performed during 2004–2006 at an intensive care unit in Hanoi. For ethical reasons the study was not randomized. All patients who fulfilled the inclusion criteria during the first two years were prospectively enrolled, carefully monitored and recorded in a predetermined study protocol, and treated with optimal supportive therapy (control group). The patients who entered the study during the third year were treated with antivenom therapy in addition to supportive care (antivenom group). The inclusion criteria were: envenomation by *B. multicinctus*, presence of systemic envenomation (neuromuscular signs), and (during the year 2006) provision of written informed consent. Predefined outcome endpoints were number of patients requiring mechanical ventilation, duration of mechanical ventilation, length of stay in the ICU, duration of muscle paralysis, and number of patients with ventilator-associated pneumonia. The antivenom was approved by the National Institute for Control of Medico Biological Products, Ministry of Health in Vietnam, and the study was approved by the Ethics Committee of Hanoi Medical University. *Results:* A total of 81 patients fulfilled the inclusion criteria. Of these, 54 patients were included during the years 2004–2005 (control group) and 27 during 2006 (antivenom group). Baseline characteristics, such as poisoning severity score on recruitment, were similar in the groups. The antivenom-group patients had a significantly shorter duration of limb paralysis and of ptosis ($p<0.001$). The duration of needed mechanical ventilation and the length of the ICU stay were also significantly shorter in the antivenom group (8.6 versus 2.3 days and 11.6 versus 6.1 days, respectively) ($p>0.001$). The rate of ventilator-associated pneumonia was lower in the antivenom group ($p<0.02$). However, the relative number of patients requiring mechanical ventilation was not reduced in the antivenom group. The rate of adverse reactions to the antivenom was 7.4%. *Conclusion:* A favourable efficacy and acceptable safety of this new antivenom were demonstrated.

241. α-amanitin-Containing Mushroom Poisoning: Outcome in 157 Patients Treated with the Triade N-Acetylcysteine, Forced Diuresis and Activated Charcoal Gastrointestinal Dialysis (Pavia Protocol)

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Objective: To evaluate the outcome of α-amanitin-poisoned patients treated with N-acetylcysteine (NAC), forced diuresis (FD) and activated charcoal gastrointestinal dialysis (GD) (Pavia protocol) apart from general supportive care. *Methods:* Retrospective evaluation of confirmed cases of α-amanitin poisoning observed from January 2002 to November 2009. Inclusion criteria were (i) positive history for mushroom consumption, (ii) laboratory confirmation of α-amanitin toxic levels (>10 ng/mL RIA, >1.5 ng/mL EMIT), (iii) treatment with the Pavia protocol including NAC (intravenous 150 mg/kg followed by 300 mg/kg/day until 48 hours after mushroom ingestion in patients without hepatitis and as long as AST <200 UI/L in patients with hepatic damage), FD until negative urinary α-amanitin levels, and GD (activated charcoal 2–5 g/h until 96 hours). Hepatic damage was defined using the acme of ALT during hospitalization: negative (ALT <49 UI/L), mild (ALT 50–199 UI/L), moderate (ALT 200–2000 UI/L), severe (ALT >2000 UI/L). Outcome was evaluated as fully recovered, organ transplantation, death. *Results:* 157 patients (age 51.9±18.5) were included. At first evaluation 119/157 (75.8%) patients presented normal hepatic function (group-1) while 15/157 (9.5%), 17/157 (10.8%), 6/157 (3.8%) presented mild (group-2), moderate (group-3) and severe (group-4) hepatic damage, respectively. Among group-1, 59/119 (49.6%) cases did not develop hepatic damage; 15/119 (12.6%), 24/119 (20.2%) and 21/119 (17.6%) patients developed mild, moderate and severe hepatic damage, respectively. In group-2, 7/15 (46.6%) patients remained with mild, 3/15 (20%) and 5/15 (33%) developed moderate and severe hepatic damage, respectively. In group-3, 7/17 (41.2%) patients remained with moderate and 10/17 (5.9%) developed severe hepatic damage. 48.3% (73/151) of the patients did not worsen after the treatment was started. NAC treatment was started from 12 to 168 hours after mushroom ingestion and was performed for 2–21 days: no adverse effects were registered. Three fatal cases and 1 case of liver transplantation were registered: the overall mortality rate (considering the transplantation a failure of medical treatment) is 2.5% (4/157). *Conclusion:* The observed mortality rate is lower than in published case series in which NAC was not used.[1] *References:* 1. Ganzert M, Felgenhauer N, Schuster T, et al. Amanita poisoning-comparison of silibinin with a combination of silibinin and penicillin. Dtsch Med Wochenschr 2008; 133:2261–7.

242. Thrombocytopenia in Envenoming by the Common European Adder, *Vipera berus*

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Objective: To report and describe significant thrombocytopenia among patients envenomed by the Common European Adder, *Vipera berus*. *Methods:* Consultations to the Swedish Poisons Information Centre during 1995–2009 concerning patients envenomed by *V. berus* were reviewed with regard to the occurrence of thrombocytopenia ($<150\times10^9$/L). Complementary data from the respective hospitals were collected. The severity of poisoning was assessed using the Poisoning Severity Score.[1] *Results:* During the study period 944 hospital case records regarding patients bitten by *V. berus* were received. Thrombocytopenia was noted in 36 cases and developed with a median latency time of 2–3 days. However, in 19 patients thrombocytopenia was present within the first hours after the bite. Eight patients had platelet counts below 50×10^9/L, three of whom $\leq 20\times10^9$/L and

one patient even below 5×10^9/L. Six of these patients with extreme thrombocytopenia were children less than ten years old. The response to antivenom (ovine Fab) treatment was highly variable. Out of 27 patients treated, no effect or transient effect was seen in 20 cases whereas normalisation followed in seven patients, two of whom had received repeated doses. Persistent thrombocytopenia up to 4–8 days after the bite was noted in 11 cases, nine of which had been given antivenom. Other coagulation abnormalities were minor or moderate, consisting of prolongation of INR/APTT, hypofibrinogenemia and elevated levels of D-dimers. No bleeding was reported. Envenoming was classified as severe (PSS 3) in 44% of the patients and moderate (PSS 2) in 50%. In most patients the oedema involved the whole extremity (n = 17) or even parts of the trunk (n = 17). *Conclusion:* Bites by the Common European Adder may, although rarely, result in significant thrombocytopenia occurring either within a few hours or after 2–3 days. The response to antivenom treatment is unpredictable and variable. The underlying mechanisms seem obscure and are presumably multiple. A hypothesis could be that early thrombocytopenia is caused by a direct effect of the venom, leading to a sequestering of platelets from the blood, while a low platelet count later on is due to loss of thrombocytes into the injured tissues. *References:* 1. Persson HE, Sjöberg GK, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol 1998; 36:205–13.

243. The Major Solvent in Agricultural Dimethoate Preparations is Essential for Toxicity in Minipigs

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Introduction: Dimethoate poisoning is a major clinical problem in rural Asia. Unlike poisoning with other organophosphorus insecticides, many deaths result from cardiovascular shock after early respiratory failure. The reason for this different clinical presentation is unclear. We established a pig model to explore the pathophysiology of this poisoning. *Methods:* Gottingen minipigs were anaesthetized before being poisoned with agricultural dimethoate (40% emulsifiable concentrate [EC40]), dimethoate 25% active ingredient in ethanol, and/or cyclo-hexanone. Atropine, pralidoxime, norepinephrine and fluids were administered as required for twelve hours. Blood was taken for pharmacokinetic/dynamic studies and biochemistry; neuromuscular function was assessed by mechanomyography, alveolar-capillary barrier function by bronchoalveolar lavage. *Results:* 2.5 mL/kg dimethoate EC40 caused severe hypotension due to peripheral vasodilatation that was similar to human poisoning. High norepinephrine doses were required to maintain a mean arterial pressure >55 mmHg; this requirement was associated with an elevated arterial blood lactate (15 mmol/L). Red cell acetylcholinesterase (AChE) activity fell to <20% of normal by 4 hours; there was minimal response to pralidoxime. Neuromuscular function failed by 12 hours; disruption of the lung alveolar-capillary barrier was noted by 4 hours. 1.25 mL/kg dimethoate EC40 caused identical inhibition of red cell AChE and neuromuscular failure, but no severe hypotension or hyperlactataemia. Dimethoate active ingredient alone inhibited red cell AChE but caused only moderate hypotension and hyperlactataemia, and no neuromuscular failure. The addition of cyclohexanone to dimethoate active ingredient reproduced the full toxic syndrome. *Conclusion:* This study shows that coformulants are essential for dimethoate toxicity; reformulation of OP pesticides may therefore rapidly reduce the number of deaths. We also found that severe red cell AChE inhibition (to less than 20% of normal activity) is not necessarily associated with severe cardiovascular toxicity. Disruption of the alveolar-capillary barrier by blood-borne dimethoate suggests that acute lung injury may explain some of the late deaths that occur in ventilated patients.

244. Therapeutic Effects of Sodium Bicarbonate and Magnesium Sulphate in Organophosphate Poisoning: A Randomized Clinical Trial

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Objective: Organophosphate (OP) pesticides are widely used in agricultural settings. Intentional and accidental overdoses with these agents are common in this country.[1] This study was aimed at comparing the therapeutic effects of sodium bicarbonate and magnesium sulphate on organophosphate poisoning. *Methods:* All consenting subjects with alleged moderate to severe acute organophosphate poisoning from May 2008 to September 2009 were studied prospectively. Ethics approval was obtained (MUMS-84386). These subjects were randomly allocated into 4 groups 1. sodium bicarbonate (S). 2. magnesium sulphate (M) 3. both (B) and 4. none (N). All cases received fluids and atropine as well as diazepam if needed. *Results:* 27 S, 25 M, 27 B and 26 N subjects were studied. Age, gender, addiction and severity of poisoning were not significantly different in these four groups. There were no significant differences in atropine administration, mechanical ventilation, ICU admission and deaths in these groups. Magnesium sulphate significantly reduced mean duration of admission ($P = 0.041$), diazepam administration ($P = 0.015$) and seizure ($P = 0.003$). *Conclusion:* This study does not support previous findings in regard to beneficial effects of sodium bicarbonate,[2] which might be due to limited power of the study. It suggests that magnesium sulphate may prevent seizures, reduce the need for diazepam administration and decrease duration of admission. Further studies in this regard are warranted. *References:* 1. Afshari R, Majdzadeh R, Balali-Mood M. Pattern of acute poisonings in Mashhad, Iran 1993–2000. J Toxicol Clin Toxicol. 2004; 42:965–75. 2. Balali-Mood M, Ayati MH, Ali-Akbarian H. Effect of high doses of sodium bicarbonate in acute organophosphorous pesticide poisoning. Clin Toxicol (Phila) 2005; 43:571–4.

245. Clinical Effects Reported in Apparent Peanut Poisoning in Dogs - A Real Mixed Bag

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Objective: Peanuts (*Arachis hypogaea*) are considered of low toxicity to most animal species. However, cases reported to the Veterinary Poisons Information Service (VPIS) indicate that some dogs become unwell after peanut ingestion. This study examines the clinical effects associated with ingestion, comparing details of asymptomatic and symptomatic populations. *Methods:* Essential details from each telephone enquiry VPIS receives are documented contemporaneously. Further data on subsequent clinical course and outcomes are elicited by postal follow-up questionnaires. All instances of peanut ingestion by dogs, with and without outcome data, on the VPIS database were retrospectively analysed. Cases involving coingestion of other agents, like chocolate, were excluded. *Results:* Between 1996 and March 2009 37 cases with full outcome data were identified. Of these, 16 dogs remained asymptomatic and 21 became unwell. Of the latter, 14 developed gastrointestinal effects and 7 exhibited increased neuromuscular activity (hyperaesthesia, twitching, tremors, or convulsions). Other unusual effects documented included anaemia, hallucinations, DIC and hepatic injury. Two fatalities were reported; all other animals made a full recovery. VPIS consultations about animals that remained asymptomatic occurred earlier, at a mean time of 50 minutes post ingestion (n = 9). These animals had a mean age of 3.9 years (n = 13) and a mean weight of 13.4 kg (n = 13). Enquiries about dogs that became symptomatic occurred at a mean time of 25 hours post ingestion (n = 10). These had a mean age of 7.47 years (n = 20) and a mean weight of 19.3 kg (n = 18). In most cases the quantities of peanuts ingested remained unknown. Where known, quantities varied from 1 "handful" to 2 kg. Analysis of cases without follow-up data showed that at the time of contact with VPIS a further 12 dogs reportedly had gastrointestinal effects, 3 exhibited signs of increased muscular activity and 2 had signs of hepatic damage. *Conclusion:* The exact cause(s) of the effects remain unknown. Explanations could include contamination of peanuts with aflatoxins, fungi or other compounds, possible salt toxicity or idiosyncratic reactions. Symptomatic animals tended to be older and larger than those remaining asymptomatic. Follow-up and analysis of further cases is needed to determine any statistically significant predispositions in dogs.

246. The Fetal Effects of Ibuprofen Overdose in the Third Trimester of Pregnancy and the Risk of Premature Closure of the *Ductus Arteriosus*

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Objective: There are limited published data on fetal outcomes following ibuprofen overdose in pregnancy, especially after third trimester exposure. NSAIDs are not recommended as therapy after week 30 of pregnancy due to the risk of premature closure of the *ductus arteriosus* (DA) and associated complications such as fetal cardiac failure or persistent pulmonary hypertension in the newborn. This on-going prospective case series aims to collect data and assess the potential fetotoxic effects of ibuprofen overdose during the third trimester pregnancy. *Methods:* Using standardised procedures, the UK Teratology Information Service has provided risk assessment and collected outcome data on a prospective case series of women exposed to ibuprofen in overdose during the third trimester of pregnancy. Overdose was defined as documented ingestion of more than the maximum daily therapeutic amount (2.4 g). *Results:* There were 16 confirmed cases of third trimester ibuprofen overdose, of which 12 were also exposed to other medications. The total amount of ibuprofen ingested ranged from 3.2 g to 28 g. All 16 infants were liveborn and two had complications due to suspected ductal constriction (12.5%; 95%CI 2.2–39.5) after maternal overdose with ibuprofen in monotherapy. No congenital malformations were observed in this data series. The first was an infant delivered at 34 weeks who had confirmed constriction of the DA after maternal ingestion of at least 6 g ibuprofen at week 30 of pregnancy. The second infant was delivered by emergency caesarean section at week 37 of pregnancy, 36 hours after maternal ingestion of 7.2 g ibuprofen, and had suspected premature closure of the DA at birth. *Conclusion:* Use of ibuprofen after week 30 of pregnancy may be associated with a risk of premature closure of the DA. The minimum dose, or duration of treatment associated with this has not been established. However, these data suggest that a single relatively modest exposure during this period may be associated with risk - even in the absence of maternal toxicity. Detailed fetal investigation including a fetal Doppler echocardiogram is recommended in third trimester ibuprofen overdose as antenatal identification of premature closure of the DA may be an indication for expedited early fetal delivery.

247. Outcome of Antiepileptic Drug Treated Pregnant Women

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Objective: To evaluate antiepileptic drug therapy during pregnancy. *Methods:* 289 epileptic women (group A) and 245 patients affected by psychiatric disorders

(group B) treated with antiepileptic drugs (AEDs) during pregnancy were studied in comparison with 1050 healthy pregnant subjects (group C). *Results:* A higher miscarriage rate was found in group B vs both group C (OR: 3.47, CI: 2.2–5.5) and group A (OR: 1.92, CI 1.1–3.34). Moreover, elective termination of pregnancy occurred more frequently in group B versus C (OR: 30.58, CI 13.53–69.14) and group A (OR: 5.58, CI: 2.72–11.41). Epileptic patients showed significant differences versus controls as regards to higher caesarean section rate (OR: 2.06, CI: 1.54–2.76), head circumference below 3rd percentile (OR: 3.17, CI: 1.51–6.67) and higher incidence of low birth weight (OR: 2.13, CI: 1.29–3.52), respectively. Apgar score and prematurity have not shown any statistical difference among the considered groups. A statistically significant increase of major congenital malformation (MCM) was shown only between group A and controls. Polytherapy was an aggravating factor in either group A and B concerning MCM rate versus controls with only the former group reaching significance (OR: 2.66, CI: 0.99–7.19). *Conclusion:* The study shows an overall tendency of developing "adverse effects" in pregnancy whenever an AED is administered. The higher frequency of miscarriages encountered in group B may be correlated to other individual risk factors like recreational substances (smoking, alcohol, coffee and drug of abuse). Besides the above mentioned polydrug regimen encountered in 93.06% of cases, which has been proved to be a risk factor for spontaneous abortion, epileptic patients showed a higher risk rate of caesarean section, low birth weight babies, lower head circumference below 3rd percentile and major congenital malformations. These data suggest the hypothesis that many factors such as drugs, epilepsy *per se* and individual factors, namely genetic ones, induce the observed adverse effects in pregnancy.

248. Pharmacotherapy for Heart Rate Control in Patients with Cocaine Associated Chest Pain Undergoing Coronary Computed Tomography Angiography

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Objective: Cocaine-associated chest pain is a common complication of cocaine use. Cocaine induced vasospasm of the coronary arteries may cause acute coronary syndromes (ACS). Coronary computed tomography angiography (CTA) is being utilized to evaluate low risk patients to exclude ACS.[1] For optimal angiography, the heart rate must be slow; metoprolol is often given. In patients with cocaine associated chest pain, beta-receptor antagonists are considered risky due to unopposed alpha-receptor mediated vasoconstriction. We describe our experience in rate control therapy in patients with cocaine associated chest pain undergoing coronary CTA. *Methods:* Consecutive patients with cocaine associated chest pain who underwent coronary CTA between March 2006 and July 2009 were studied. ED clinicians determined the necessity and therapy utilized for rate control. *Results:* 112 patients underwent coronary CTA. The average age of the patient was 45.1 ± 6.8 years, 64% male. The mean (± SD) heart rate on presentation was 85.1 ± 15.2 (range 51–132 beats/min). 36 patients received benzodiazepines and had heart rate reduction from 89.7 ± 15.6 to 74.6 ± 10.8 beats/min; 17 patients received calcium channel antagonists and had heart rate reduction from 97.1 ± 11.8 to 80.8 ± 8.8 beats/min; 27 patients received beta receptor antagonists and had heart rate reduction from 89.8 ± 14.5 to 73.6 ± 12.8 beats/min and in systolic BP from 136.8 ± 23.4 to 128.8 ± 16.2 mmHg prior to coronary CTA. 51 patients had heart rates 79 ± 14 beats/ min but decreased to 66.5 ± 13.8 beats/min without specific rate control therapy and underwent coronary CTA. No adverse events occurred immediately or during hospitalization. *Conclusion:* In a cohort of patients with cocaine associated chest pain undergoing coronary CTA, rate control was achieved with benzodiazepines, calcium channel or beta-receptor antagonists. The optimal therapy in this setting requires further evaluation.

References: 1. Walsh K, Chang AM, Perrone J, et al. Coronary computerized tomography angiography for rapid discharge of low-risk patients with cocaine-associated chest pain. J Med Toxicol 2009; 5:111–9.

249. The role of Computerized Tomography as a Diagnostic Tool for Evaluating Caustic Injury

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Objective: To evaluate the role of computerized tomography (CT) in the diagnosis and therapeutic decision making of patients with caustic ingestion. *Methods:* A retrospective chart review of patients admitted after caustic ingestion to surgical wards in a tertiary care hospital between 2000 and 2008. Demographics, type of caustic, time elapsed from ingestion, circumstances of exposure, admission physical examination, laboratory evaluation, chest and abdomen x-ray and CT, and upper gastrointestinal endoscopy findings were abstracted. Endoscopy findings were graded as grade 0, 1, 2A, 2B, 3A and 3B, according Zargar's criteria.[1] CT findings were graded as grade 0 (normal appearing organs) grade 1 (edematous wall thickening), grade 2 (grade 1 and soft tissue infiltration), and grade 3 (grade 2 and air bubbles in organ wall/free mediastinal or abdominal air/fluid collection). Data were subjected to descriptive analysis. *Results:* 39 patients were included; mean age 40.8±16.9 years, 16 males, and 30 intentional ingestions. Caustics involved were acids (14), alkalis (9), bleaches (13) and others (3). Both CT and endoscopy were preformed in 11 patients (seven alkali, three acids, one other); all within 48 hours. Endoscopy revealed grade 1 injury (1), grade 2A (2), grade 3A (6), and grade 3B (1). In another patient the upper esophageal sphincter could not be intubated due to severe edema; he was excluded. CT findings: grade 0 in one, grade 1 in six, grade 2 in one, and grade 3 in three patients. In seven patients the severity of the CT grade was lower than the endoscopy grade, in three patients they were comparable. *Conclusion:* Chest and abdomen CT tends to underestimate the degree of caustic injury. Endoscopy grades 1 to 3A can show in CT only as edematous wall thickening (CT grade 1). It is suggested that in the initial phase of caustic ingestions surgical decisions should not be made based only on CT, unless endoscopy is not feasible or in the presence of free air. *References:* 1. Zargar SA, Kochhar R, Mehta S, et al. The role of fiberoptic endoscopy in the management of corrosive ingestion and modified endoscopic classification of burns. Gastrointest Endosc 1991; 37:165–9.

250. Successful use of Intravenous Fat Emulsion in Severe Poisoning Following Ingestion of Lipid Soluble Drugs

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Objective: Intravenous fat emulsion (IFE) has been successfully used as an antidote in cases of local anaesthetic toxicity and the possibility of its usefulness in overdose of other lipid-soluble drugs continues to provoke interest. We report a case of a mixed overdose where IFE was given successfully to treat a haemodynamically compromised patient. *Case report:* A 52 year old female was admitted to A&E three hours after ingestion of amitriptyline (350 mg), diltiazem SR (1680 mg), dihydrocodeine (840 mg), temazepam (70 mg), diazepam (35 mg) and citalopram (70 mg). She presented with features of calcium channel blocker toxicity; pulse 38, blood pressure 80/50, RR 10, GCS 8/15, and ECG showing complete heart block. Despite receiving conventional treatment - saline, naloxone, atropine, calcium gluconate and sodium bicarbonate she showed no improvement and required admission to the intensive care unit for ventilatory and inotropic support. Awaiting transfer to ITU, 20% intralipid (500 mL) was administered over 30 minutes. Her post-lipid ECG showed sinus rhythm, pulse 79, PR 191, QRS 107 ms, QT/ QTc 407/467 ms. Her blood pressure on admission to ITU was 124/55 mmHg. She subsequently continued to improve requiring no inotropic support and was extubated the following day. A mild aspiration pneumonia was treated successfully with co-amoxiclav and she was discharged after psychiatric assessment without sequelae. *Conclusion:* Animal studies have demonstrated a reduction in morbidity and mortality from lipid-soluble drug cardiotoxicity with IFE, and in humans it has been used to treat local anaesthetic toxicity, as well as bupropion/lamotrigine toxicity. Its exact mode of action is unclear but it may trap lipophilic drugs in an expanded plasma lipid compartment (lipid sink).[1] This case demonstrates the successful use of IFE in an overdose involving amitriptyline and diltiazem. Administration of intralipid rapidly reversed ECG changes and improved haemodynamic status without the need for inotrope therapy or extended ITU support. Although data from human poisonings are still limited, we believe there is a role for IFE therapy in managing patients with overdose from lipid-soluble drugs. *References:* 1. Sirianni AJ, Osterhoudt KC, Calello DP, et al. Use of lipid emulsion in the resuscitation of a patient with prolonged cardiovascular collapse after overdose of bupropion and lamotrigine. Ann Emerg Med 2008; 51:412–5.

251. Evaluation of the Management of Overdoses of Digoxin

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Objective: Recent data on digitalis poisonings and overdoses show the importance of Digoxin-specific Fab fragments (Fab) as a first line treatment. In order to assess our professional practices, we decided to analyze (from December 2008 to September 2009), the management of all digoxin overdoses in Rodez General Hospital (France, Aveyron). *Methods:* Prospective observational study. Main criteria: indication of treatment with Fab according to expert recommendations. Secondary endpoints: i) further prescription; ii) inpatient unit admission; iii) mortality. *Results:* Cohort of 39 cases (see Table 1). Median age 84 years [63, 99], ratio M/F 0.63. Three case reports were excluded for lack of clinical data. Further prescription: 59% withdrawal of digoxin; 77% ECG; 33.3% telemetry; 2.6% atropine. Inpatient unit: 46% medicine; 23% ICU; 13% discharged

Table 1. Cohort of 39 cases

		Recommendation of treatment with Fab		
	Number of records	Molar	Half-molar	No
population not treated with Fab	33	14 (38.9%)	17 (47.2%)	2 (5.5%)
population treated with Fab	3	2 (5.5%)	0	1 (2.8%)

(outpatients); 10% surgery; 8% emergency care unit. Mortality rate 17.9%. *Conclusion:* The management of digitalis overdose does not match with experts' recommendations. Fab fragments, as with other treatments, are underutilized. It would be interesting to remind staff of the guidelines for digoxin overdose then to re-evaluate the quality of this management.

252. Hemodynamic Effects of Insulin and Dextrose in Healthy Volunteers

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Objective: The combination of high dose insulin and glucose has been repeatedly used in various cardiac conditions (chronic heart failure,[1] acute myocardial infarction,[2] cardiac surgery[3]) and has become part of the antidotal treatment of overdose with calcium channel and beta-adrenergic blocking agents.[4] Little, however, is understood about the drug interactions at the myocyte level and various hypotheses have been generated to explain the cardioprotective mechanism of insulin/glucose in the stressed myocardium. With this study we tried to understand the effects of insulin-euglycemia treatment on hemodynamics of healthy hearts *in vivo*. *Methods:* Ten healthy females were enrolled in a prospective double blind cross-over trial. Each volunteer received 10 units regular insulin with 25 gm dextrose IV vs. placebo (0.9% saline IV). After each infusion cardiac parameters (heart rate, blood pressure, fractional shortening of the left ventricle) were measured every 15 min for one hour. ANOVA for repeated measures was calculated using insulin/glucose or placebo treatment as subject factors. *Post-hoc* paired t-tests were done when ANOVA analysis suggested a significant effect at an alpha = 0.05 level. *Results:* For heart rate (HR), systolic blood pressure (SBP), and fractional ventricular shortening (FVS) no significant differences in group means could be detected. There was a statistical significant difference towards lower diastolic blood pressures (DBP) in the insulin/glucose treatment arm (ANOVA p = 0.004). Paired t-test analysis calculated significant differences for DBP between the treatment arms at 15, 30, and 60 min (p = 0.02, 0.04, and 0.01 respectively). However, the treatment effect was measured as a decrease in DBP of only 3.9–5.4 mmHg. *Conclusion:* Low-dose insulin-euglycemia treatment seems to have little or no effect on the hemodynamic parameters of healthy, non-stressed hearts. Therefore, cardioprotective effects from insulin/glucose might be more evident with use of high-dose insulin regimens or under conditions with maximal cardiac distress. *References:* 1. Parsonage WA, Hetmanski D, Cowley AJ. Beneficial haemodynamic effects of insulin in chronic heart failure. Heart 2001; 85:508–13. 2. Malmberg K. Prospective randomized study of intensive insulin treatment on long term survival after acute myocardial infarction in patients with diabetes mellitus. BMJ 1997; 314:1512–5. 3. Svedjeholm R, Huljebrant I, Hakanson E, et al. Glutamate and high-dose insulin-potassium (GIK) in the treatment of severe cardiac failure after cardiac operations. Ann Thorac Surg 1995; 59:S23–30. 4. Kerns W. Management of beta-adrenergic blocker and calcium channel antagonist toxicity. Emerg Med Clin N Am 2007; 25:309–31.

253. Glucarpidase - A Fast and Efficient Antidote in Methotrexate Poisoning

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Objective: Methotrexate (MTX) poisoning is a complication in immunosuppressant and anti-neoplastic therapy.[1] It occurs as a consequence of high-dose therapy with renal impairment and delayed renal excretion as well as with dosage errors. It has been shown, that intravenously injected bacterial enzyme glucarpidase rapidly hydrolyzes MTX into inactive 2,4-diamino-N10-methylpteroic acid (DAMPA) and glutamic acid, thus abrogating toxicity of MTX.[2] Hitherto, the analytical monitoring of this effect has been obscured because immunoassays crossreact with DAMPA yielding false high readings for MTX. Therefore a LC-MS/MS method has been developed to quantify the degradation of MTX and the formation of DAMPA *in vivo*. In addition, we performed kinetic *in vitro* studies to explore enzymatic activity. *Methods:* The analytical method consisted of a liquid chromatography on phenylhexyl column, 50 mm×2.0 mm, 5 µm (Phenomenex) and MS/MS-detection of the analytes MTX, 7-hydroxy-MTX and DAMPA using the multiple reaction mode on a QTRAP 3200 (Applied Biosystems). Lower limit of quantification was 4.4 nmol/L with a linear range up to 4.4 µmol/L for MTX. *Results:* (A) Human blood samples spiked with 4.4 µM/L MTX were treated with glucarpidase (0.75 U/L) at 37 °C. Concentration of MTX dropped below 0.4 µmol/L within five minutes with proportional increases of DAMPA concentrations above 4.0 µM/L. (B) The time course of MTX concentrations from two patients receiving MTX (5,000 mg/qm, or 12,500 mg/qm) revealed the degradation of more than 95% of MTX before the first sample was drawn 45 min after i.v. application of the enzyme. *Conclusion:* Glucarpidase hydrolyzes more than 90% of MTX within five minutes producing an equivalent amount of DAMPA *in vitro* and probably *in vivo*. Commercially available immunoassays are unsuitable for monitoring the success of MTX-degradation after glucarpidase rescue treatment requiring a refined analytical approach. Glucarpidase appears to be a fast acting and safe antidote in the treatment of methotrexate intoxication. *References:* 1. Peyriere H, Cociglio M, Margueritte G, et al. Optimal management of methotrexate intoxication in a child with osteosarcoma. Ann Pharmacother 2004; 38:422–7. 2. Mohty M, Peyriere H, Guinet C, et al. Carboxypeptidase G2 rescue in delayed methotrexate elimination in renal failure. Leuk Lymphoma 2000; 37:441–3.

254. An Anticalin with Drug-Binding Properties: Results of a Pilot Study to Reverse Digoxin-Toxicity in Rats

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Objective: To evaluate the properties of an engineered lipocalin to serve as a specific digoxin-binding antidotal therapy in a pilot study in rats. *Methods:* Intravenous digoxin (50 µg/kg/min) was administered continuously to anesthetized and artificially ventilated rats until first changes in the ECG occurred (e.g. conduction-delays, bundle branch block). A specifically engineered lipocalin with high affinity for digoxin, the Anticalin DigA16(H86N), was administered intravenously at doses of 1, 5, 10 and 19 mg, respectively. These animals were compared with a group receiving isotonic saline instead. Hemodynamic changes, several ECG-parameters as well as digoxin concentrations in serum were monitored continuously until death or when the animals were euthanized (usually 210 min after start of digoxin infusion). Digoxin in serum was determined at given time intervals prior to Anticalin administration using the Abbott® and EMIT®-assay, respectively. Following Anticalin injection, free digoxin was determined in serum ultrafiltrate using the same assays. *Results:* Treatment groups did not differ significantly in physiological and baseline parameters. There was a clear trend to longer survival, later occurrence or absence of arrhythmia, minor decrease in mean arterial pressure, and shorter PQ-, QRS- and QTc-intervals of animals receiving higher doses of Anticalin compared to the low-dose or placebo group. Infusion of a lower digoxin dose (e.g. 5 µg/kg/min) resulted in a more sustained reduction of free digoxin in serum, whereas ECG- and hemodynamic parameters did not relevantly differ in agreement with the known relative insensitivity of rats towards digoxin toxicity. Notably, we observed a reincrease of free digoxin in serum after bolus administration of the Anticalin, which was presumably due to its fast renal clearance. *Conclusion:* An engineered binding protein based on the lipocalin scaffold was shown to reduce digoxin toxicity in a rat model. Thus, Anticalins with appropriately engineered drug-binding activities and, possibly, prolonged plasma half-life offer prospects for next-generation antidotal therapy. *References:* 1. Schlehuber S, Beste G, Skerra A. A novel type of receptor protein, based on the lipocalin scaffold, with specificity for digoxigenin. J Mol Biol 2000; 14:1105–20.

255. Severe Formalin Accident Poisoning: A Case Report

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Objective: Ingestion of formalin is rare but often leads to death. A therapeutic approach is discussed including N-acetylcysteine (NAC). We propose that treatment with N-acetylcysteine (NAC) may contribute to the hepatic detoxification after formalin ingestion. In fact, the oxidation of absorbed formaldehyde to formic acid is catalyzed by the NAD-dependent formaldehyde dehydrogenase, which requires reduced glutathione as a cofactor and NAC, a glutathione precursor, might help to maintain or replenish the level of the hepatic reserves. Thus, we report a case illustrating the favorable outcome after formaldehyde ingestion with treatment by NAC and intensive care. *Case report:* A 40 year old man presented to an emergency department after taking an indefinite amount of formalin. The initial status included respiratory failure, circulatory failure, hyperthermia, elevated liver enzymes and coagulopathy. Emergency oesophagogastric endoscopy disclosed corrosive gastric and oesophageal injuries. Medical therapy consisted of mechanical ventilation, and noradrenaline. N-acetylcysteine was recommended and delivered by the Poison Control Centre. The respiratory and hemodynamic status improved, the patient was successfully extubated after 5 days, and had a subsequent resolution of the hepatic cytolysis 11 days after the intoxication. *Conclusion:* The use of NAC appeared to allow the fast improvement to the hepatic cytolysis in this patient and contributed, with the intensive care, to the good outcome. It is important to identify the exact role of NAC in formaldehyde intoxication in order to clearly elucidate its mechanism of action. This will require the use in similar cases and experimental studies.

256. A Cost Analysis of Treating Patients with Ethylene Glycol Poisoning with Fomepizole Alone Versus Hemodialysis and Fomepizole

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Objective: We sought to compare the costs of fomepizole alone versus hemodialysis plus fomepizole in treating an ethylene glycol poisoned patient, based on the initial serum concentration of ethylene glycol and patient body weight. *Methods:* Patient charges were calculated based on fees charged at a US tertiary care, academic hospital. Costs for fomepizole only include the cost of fomepizole (given at 15 mg/kg once followed by 10 mg/kg every 12 hours), admission to the ICU at high ethylene glycol levels, followed by transfer to a general medical unit, and laboratory testing. Costs for hemodialysis plus fomepizole included the cost of fomepizole, admission to the ICU for the first day followed by the general medicine unit, nephrology consultation, insertion of a Quinton catheter, chest radiograph to confirm catheter placement; one four-hour session of dialysis every 24 hours; and laboratory tests while being treated until ethylene glycol concentrations fell below 25 mg/dL. Calculations were based on a 75 kg patient (mean weight for an

adult female in the US), for an 87 kg patient (mean weight for an adult male in the US), and for an individual weighing greater than 100 kg. We assumed normal renal function and previously published ethylene glycol elimination half-lives during hemodialysis and during fomepizole. *Results:* At weights up to 75 kg, the cost analysis favors treating patients with fomepizole alone at all ethylene glycol concentrations, except for initial ethylene glycol concentrations between 500 and 600 mg/dL. For a patient weighing between 75–100 kg, the cost of treatment is almost equivalent up to 300 mg/dL, but above this concentration combined hemodialysis and fomepizole become less expensive. For a patient weighing greater than 100 kg, it is more cost effective to treat the patient with both hemodialysis and fomepizole when the initial ethylene glycol level is greater than 75 mg/dL. *Conclusion:* In patients with normal creatinine clearance, combined treatment with hemodialysis and fomepizole is less expensive for patients with a larger body mass. Treatment with fomepizole alone is less expensive for patients with a small body mass.

257. The Availability of 'Lipid Rescue' Therapy for Local Anaesthetic Toxicity to Anaesthetists in Belgium

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Objective: To evaluate the availability of lipid emulsion therapy for local anesthetic toxicity to anaesthetists in Belgium. *Methods:* We contacted by email the head of the department of anaesthesiology of each hospital registered as 'general hospital', 'general hospital with university character' and 'university hospital' (cfr. http://www.hospitals.be). They were asked to complete a survey on a website (http://www.surveymonkey.com). *Results:* 125 anaesthetists, covering 192 hospitals (some of whom are head of the department in more than one hospital), were contacted. We received replies from 69 (55%) anaesthetists responsible for 98 (51%) hospitals. 'Lipid rescue' was available to patients receiving potentially toxic doses of local anaesthetics in 54/98 (55%) responding hospitals. The main reason for adopting lipid emulsion as a rescue therapy was the publication of the guidelines recommending lipid rescue for the treatment of local anesthetic toxicity by the Association of Anaesthetists of Great Britain and Ireland (AAGBI). In most cases the head of the department took the decision to introduce the 'lipid rescue pack'. *Conclusion:* In autumn of 2009 'lipid rescue therapy' was available in the operating department, recovery area or labour ward in only half the Belgian hospitals. In Belgium the publication of the AAGBI guidelines has less impact on the availability of lipid rescue therapy as compared to the study made by Picard in Great Britain and Ireland.[1] *Reference:* 1. Picard J, Ward SC, Zumpe R, Meek T, Barlow J, Harrop-Griffiths W. Guidelines and the adoption of 'lipid rescue' therapy for local anaesthetic toxicity. Anaesthesia. 2009 Feb;64(2):122–5.

258. Use of High-Dose *Crotalidae* Polyvalent Immune Fab in a Toddler with Copperhead Envenomation

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Objective: The safety of *Crotalidae* polyvalent immune Fab (Crofab) for copperhead envenomations has not been studied in pediatric patients. This report documents the safety of high dose Crofab in a toddler bitten by a copperhead. *Case report:* A 28-month-old female was bitten on her right knee by a copperhead while playing in her backyard. Her father positively identified the snake, and the patient was transferred to an academic medical center (AMC) after brief evaluation in an outside hospital. On initial evaluation at the AMC (about 4.5 hours after the bite), the patient's right leg was noted to be ecchymotic and swollen from the ankle to the hip, with a right thigh circumference roughly three times greater than the left. Peripheral pulses were diminished and capillary refill was delayed. She was immediately treated with four vials of Crofab and the leg was elevated. Her vital signs and initial laboratory studies were normal, with exception of fibrinogen (149 mg/dL) and WBC (19,800 u/L). She was admitted to the ICU where swelling of her right lower extremity progressed to her umbilicus and both labia. The patient received an additional 18 vials over 24 hours to impede swelling and improve right lower extremity perfusion. Her edema significantly decreased by day three and she was discharged on day seven. No adverse reactions to Crofab were identified. *Conclusion:* Crofab is effective in treating copperhead envenomation in adults.[1] Limited data is available on Crofab use in children.[2] This case demonstrates uncomplicated use of high dose Crofab in a pediatric patient with progressive edema following copperhead envenomation. *References:* 1. Lavonas EJ, Gerardo CJ, O'Malley G, et al. Initial experience with crotalidae polyvalent immune Fab (ovine) antivenom in the treatment of copperhead snakebite. Ann Emerg Med 2004; 43:200–6. 2. Trinh H, Hack JB. Use of Crofab® antivenin in the management of a very young pediatric copperhead envenomation. J Emerg Med 2005; 29:159–62.

259. Antidotal Treatment of Heroin Overdose Patients

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Objective: The aim of the present study was to estimate critically the currently available antidotal treatment for heroin overdoses by heroin addicts. *Methods:* We have made a retrospective analysis of 88 patients (men), currently heroin addicts, treated at our clinic in the last five years. The group was divided into two subgroups. One group of 59 heroin overdose patients with depressed mental status such as somnolence and stupor, but without respiratory depression and the second group of 29 patients with coma status, with pinpoint pupils and respiratory depression (respiratory rate less than 12 breaths/min). All patients' routine biochemical tests were determined: blood tests, serum transaminases, ALT, AST, LDH, GGT, CPK, Alk. phosphatase, bilirubin and its fractions, urine, alkali-acid status and markers of hepatitis A, B, C and HIV. Urine concentrations of opiates were determined using fluorescence polarization immunoassay (FPIA) technique. *Results:* In the first group of patients the initial dose of intravenous injection of naloxone was 0.4 mg. A repeated dose of naloxone after two minutes was effective in mental status change to full consciousness. The third dose of naloxone in these patients caused side effects of naloxone such as anxiety, agitation and first signs of withdrawal. In the second group of patients with respiratory depression, initial dose of naloxone was 2.0 mg. Artificial ventilation was applied in four patients. Repeated doses of naloxone at one hour intervals as slow continual intravenous infusions (2.0 mg diluted in 500 mL of isotonic saline) were infused over 6 hours. The total doses (18 ampoules of 0.4 mg - 7.2 mg) of naloxone to full consciousness were injected. The duration of treatment varied up to 10 hours. Urine concentration of opiates determined with FPIA technique were up 1000 ng/mL. *Conclusion:* For the patients with depressed mental status but no respiratory depression, a total dose of 0.8 mg was effective in a short time. In the other group much greater doses were needed to achieve full consciousness and longer time for the treatment. *References:* 1. Varagic V, Milosevic M. Pharmacology. Belgrade 2007; 207–14. Elit.Medica.Serbia. 2. Strang J, Manning V, Mayet S, et al. Overdose training and take-home naloxone for opiate users: prospective cohort study of impact on knowledge and attitudes and subsequent management of overdoses. Addiction 2008; 103:1648–57. 3. Monov A. Clinical Toxicology, Sofia 1995. Volume II: 171–173. Editor Venel, Sofia, Bulgaria

260. Non-Fatal Self-Poisoning by Low Molecular Weight Heparin and the Use of Antidote

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Objective: Since protamine sulphate has been reported to incompletely balance the anticoagulation effect of low-molecular-weight heparins (LMWHs), its antidotal effect has been questioned. We report such an unusual poisoning where the effect of protamine sulphate could be evaluated. *Case report:* A 40-year old female was admitted after subcutaneously injecting herself with 17 doses of 12,500 IE (totally 212,500 IE) dalteparin in a suicide attempt. She also ingested small amounts of promethazine, citalopram, lamotrigine and acetylsalicylic acid. On admission, she was somnolent and had a GCS of 12. Circulation and respiration were stable, there were no petecchiae, but the abdominal skin showed 16–17 bleeding injection sites. Neurological examination and CT scan were normal. She received 500 mg protamine sulphate intravenously over 100 minutes. Hemoglobin was stable. APTT (STAPTT Automate 5, Diagnostica Stago) at admission was >180 seconds, i.e. over the testing limits. Anti-Xa activity was 4.40 (therapeutic range 0.5–1.0 U/mL). After receiving 500 mg protamine sulphate, APTT five hours later was 53 (normal range 27–40 s) and anti-Xa was 1.90. However, twelve hours later the APTT was >180 again, and a repeated dose of antidote was given. APTT was then normalized. After 48 hours of observation, no bleeding complications were observed. APTT and anti-Xa activity were within normal levels and she was discharged with psychiatric follow-up. To neutralize LMWH, 10 mg protamine sulphate per 1000 IE LMWH is recommended. Accordingly, 2125 mg protamine sulphate would be needed, but the given dose of 500 mg initially proved sufficient to give a clinically significant reduction of anticoagulant activity. However, protamine sulphate has a shorter half-life than LMWH, and another dosage was needed in order to balance off the anti-Xa activity. Protamine sulphate proved to be effective (with regards to APTT) in this case, as no major bleeding complications was observed. *Conclusion:* Self-poisonings by LMWH can be treated by administration of protamine sulphate, but the dosage needed to balance the anticoagulation effect is not linear according to this case report. Careful monitoring of APTT and anti-Xa activity helped guide the administration of antidote.

261. Is Digitalis Antidote Life-saving in Case of Intoxications with *Taxus baccata*?

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Introduction: It is well known that severe poisonings with yew (*Taxus baccata*) are mainly due to the toxicity of the alkaloid taxin B which can cause life threatening ventricular arrhythmias. An effective antidote is not available. A few reports about successful therapeutic trials with lidocaine[1], amiodarone, and digitalis antitoxin[2] have been published. *Case reports:* A) An 18-year old man swallowed a handful of yew leaves in a suicidal attempt. Vomiting occurred some time later; 2 hrs post ingestion he was sleepy and had ventricular tachycardia of 160/min which subsequently turned into ventricular fibrillation. The patient received ajmalin i.v., was intubated and primary detoxified. Because of ventricular fibrillation, the patient was subjected to defibrillation and subsequently received a temporary pacemaker. Assuming a substantial crossreactivity between Fab-digitalis antidote and taxins, 240 mg of digitalis anti-toxin was given i.v. which resulted in the return of sinus rhythm at normal heart rate within 1 hour. B) A 55-year old man was admitted to the hospital 16 h after the ingestion of both 150 g of yew leaves and a stock of yew leaves. Two hours post ingestion he experienced severe vomiting. On admission he was

awake but had severe hypotension and tachycardia (160–220/min), broadened ventricular complexes and acidosis (pH 7.31). He received sodium bicarbonate.[3] With recurring tachycardia (160 /min) he received 40 mg digoxin immune Fab and returned to regular sinus rhythm with normal heart rate within 30 minutes. *Conclusion:* In the two reported cases digoxin Fab antibodies terminated the taxin-induced arrhythmias. If stronger evidence for the effectiveness of digitalis antibodies in poisoning with *Taxus baccata* could be accumulated, this therapy could possibly become a standard therapy for this rare but sometimes life-threatening intoxication. *References:* 1. von Dach B, Streuli RA. Lidocainbehandlung einer Vergiftung mit Eibennadeln. Schweiz Med Wschr 1988; 118:1113–6. 2. Cummins RO, Haulman J, Quan L, et al. Near fatal yew berry intoxication treated with external pacing and digoxin-specific FAB antibody fragments. Ann Emerg Med 1990; 19:38–43. 3. Pierog JE, Kane B, Kane K, et al. Management of isolated yew berry toxicity with sodium bicarbonate: A case report in treatment efficacy. J Med Toxicol 2009; 5:84–9.

262. Outcome of Symptomatic Accidental Exposures to Wood Preservation Fungicides

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Objective: To evaluate symptomatic exposures to water based wood preservatives, containing boric acid and benzalkonium chloride, i.e. quaternary ammonium compounds (QAC), in calls to the Toxicological information Centre (TIC). The outcome of intentional ingestions may be fatal. *Methods:* A retrospective analysis of calls classified as accidental exposure to wood preservatives was performed. Data was extracted from the electronic database of TIC during 6 months (January-June 2009). Health outcome was evaluated based on discharge reports of hospitalized patients and telephone inquiries to the caller. *Results:* A total of 4485 calls were answered during the 6 months. Inquiries due to pesticides were 149 (3.3%), amongst which 23 calls about fungicides. Symptoms were noted only in 11 patients after accidental exposure to fungicides containing boric acid and QAC. In 9 subjects the follow-up was successful. There were 7 adults and 2 children. Fungicide exposures occurred after swallowing 1 sip (8 patients) or eye exposure (1 patient). First aid after exposure included washing of the mouth or eye with water (8 x), and drinking water (6 x). Fungicides were concentrated 2x, diluted 4x, unknown concentration 3x. Most frequent symptoms were burning in the mouth and throat (8x), vomiting (6x), nausea (4x) and retrosternal pain (1x). The symptoms lasted up to 20 hours. Seven patients were hospitalized for 2 days, esophagogastroscopy (EGGS) was performed in 5 patients, one patient refused it. EGGS revealed superficial damage of mucosa only. Symptomatic treatment was given in 5 patients (analgesics, intravenous fluids, oral antibiotics, and short-term corticosteroids). *Conclusion:* Accidental exposures to fungicides led to symptoms only in products containing boric acid or QAC. They had favourable outcomes in all followed cases (19% were lost to follow-up). The unpleasant taste possibly prevented a larger ingestion. First aid according to the instructions at the label of the product was undertaken shortly after exposure. Ingestion led to hospitalization in 78% and EGGS in 56% of patients. *References:* 1. Adams RD, Lupton D, Good AM, et al. UK childhood exposures to pesticides 2004–2007: a TOXBASE® toxicovigilance study. Arch Dis Child 2009; 94:417–20. *Acknowledgement:* MSM 0021620807.

263. Bystanders Acute Exposure Related to Soil Use of Metam-sodium and Metam-potassium: Observations Performed by the Italian Program for Surveillance of Acute Pesticide-related Illnesses in 2004–2009

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Objective: To describe the acute environmental exposures and the related illnesses reported to the Italian Program for Surveillance of Acute Pesticide-Related Illnesses (SAPRI-program) and attributed to soil use of methyl-isothiocyanate (MITC)-generating pesticides, including metam-sodium, metam-potassium and dazomet. *Methods:* The SAPRI-program database was searched retrospectively (January 2004-June 2009) for reports involving the chemicals of interest. The narrative section of the identified records was reviewed in order to characterise the incidents. *Results:* Five events and 110 resulting illnesses were identified. Metam-sodium was responsible in four incidents and metam-potassium in one. All the exposures occurred in summer time at about 9 p.m. The victims comprised residential bystanders (n.90) and emergency responders (n.20). Their ages ranged from <1 to 85 years. All cases were seen in or referred to a health care facility. Severity of illnesses was low. *Case series:* On July 2004, two residents of a house close to a field treated with metam-sodium complained of eye irritation. One of them reported abdominal pain. In June 2005, 1.2 acres were treated with 1,3-dichloropropene and metam-sodium by injection. Six bystanders at about 0.8 miles from the treated site were symptomatic and reported: eye irritation (n.6), vomiting (n.3), abdominal pain (n.1), tachycardia (n.1). In August 2005, 2.6 acres were treated with metam-sodium by irrigation. At the end of the application, 13 resident living 0.7 miles from the treated field developed clinical effects including: eye irritation (n.11), nausea (n.9), headache, vertigo, diarrhea (n.1, respectively). In August 2005, 0.7 acres were treated with metam-potassium by injection. At the end of the treatment four residents of a house located at less than 1 mile from the treated field reported eye irritation, nausea, and headache. In July 2009, a total of 85 residents experienced acute symptoms related to off-gassing problems from a nearby field which was treated with metam-sodium by sprinkler irrigation. The reported effects included eye and throat irritation (n.71), vomiting (n.3), headache and vertigo (n.1, respectively). *Conclusion:* The incidents related to MITC-generating pesticides are rarely documented in Europe. The observations performed in Italy indicate that adequate measures should be undertaken to reduce the risk of environmental exposures.

264. Utility of Serum Aldicarb Concentrations in Cases of Tres Pasitos Poisoning

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Objective: In our region, cholinergic poisoning from ingestion of illegally imported aldicarb-containing rodenticide, Tres Pasitos, occurs commonly. Unfortunately, because the aldicarb-cholinesterase bond spontaneously regenerates *in vitro*, confirmation and prognostication with cholinesterase activity is impractical. We studied serum aldicarb concentrations in survivors and fatalities in order to better understand the toxicokinetic/toxicodynamic profile of aldicarb poisoning. *Methods:* We searched the Medical Examiner (2005–2008) and Poison Control Center (2008–2009) databases for cases in which aldicarb poisoning was documented with a tissue concentration. These records were abstracted to gather pre- and post-mortem demographic, clinical, and analytical data. *Results:* We identified two fatal cases from the ME and three survivors from the PCC database that met inclusion criteria (see Table 1). *Conclusion:* Most aldicarb poisoning cases in the literature are not confirmed with tissue concentrations. Clinical toxicity was observed in our case series with serum concentrations as low as 0.176 mg/L, and death occurred at 1.1 mg/L. Treatment with pralidoxime was provided on the premise that the nature of the cholinesterase inhibitor had not yet been identified as an organophosphate or carbamate. Aldicarb concentrations also serve to distinguish carbamate from organophosphate poisonings and may enable judicious use of pralidoxime. Interestingly, our cases initially presented with bradycardia regardless of the oxygen saturation. The high aldicarb concentration in the patient who died

Table 1. Cases of confirmed aldicarb poisoning

Case	1	2	3	4	5
Age/Sex	47/ M	43/ F	47/ M	44/ F	60/ M
Outcome	Survived	Survived	Survived	Deceased	Deceased
Vitals					
BP	200/100	110/65	200/114	80 systolic	Slight lung congestion on the autopsy.
HR	35 bpm	46 bpm	50 bpm	30 bpm	
O_2 Saturation	90%	99%	95%	70%	
RR	14	11	22	12 (ventilated)	
Temperature	36.5 C	37.0 C	36.6 C	Unavailable	
Cholinergic Signs & Symptoms	+	+	+	Marked lung congestion on autopsy.	
Atropine Requirement	22 mg total	4 mg total	3 mg total	5 mg total	
Intubation	+	+	+	+	
2-PAM Provided	+	+	+	+	
Aldicarb Concentration	0.176 mg/L (serum)	0.47 mg/L (serum)	0.23 mg/L (serum)	1.1 mg/L (abdominal cavity fluid)	12.1 mg/L (blood) 217.6 mg/kg (gastric contents)

prior to hospital arrival may reflect incomplete distribution, limited metabolism or severe poisoning. Ongoing case collection will help describe the relationship between serum aldicarb concentrations and the toxicokinetics/toxicodynamics of aldicarb poisoning.

265. Enhanced Monitoring of Fumigant Pesticide Exposures by TOXBASE®. The NPIS Pesticide Surveillance Project 2004–2009

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Objective: To describe fumigant exposures during the 5.5 years of the NPIS TOXBASE® pesticide surveillance project. *Methods:* The National Poisons Information Service Edinburgh Unit (NPISE) monitors pesticide exposures following Internet (TOXBASE®) or telephone enquiries. All patient related accesses to pesticides of interest on TOXBASE® between 1/4/2004 and 1/10/2009 were notified electronically to NPISE, and were followed up using on-line, email or paper questionnaires. All Scottish telephone enquiries were also followed up. Enquiries from outside the UK and those where symptoms were deemed not related to the exposure were excluded. Fumigant exposures were analysed for circumstances and symptoms in adults and children. *Results:* Since 2004 4140 pesticide exposures have been reported to NPISE. Fumigant pesticides comprise a small proportion of these reports, 51 (1.2%) but frequently involve highly toxic agents such as aluminium phosphide (35, 68%), methyl bromide (15, 29%) and pirimiphos methyl (1). Most exposures involved adults (45, 88%) and all involved professional products. Twenty-five (55%) were occupational. In 15 (33%) the patients were using the product themselves, 7 (16%) use by someone else, 19 (42%) were exposed after application and 4 (9%) as a result of unsatisfactory storage. Six exposures involved deliberate self-harm (DSH) and 1 was an alleged poisoning by a third party. Seventeen (33%) of patients were asymptomatic and graded PSS[1] "none". Of the remainder: 20 "minor", 5 "moderate", 3 "uncertain", 6 "fatal". Of fatal cases 5 were DSH and 1 followed alleged poisoning by a third party, and all involved aluminium phosphide. Common symptoms in accidental exposures were: bronchospasm (10), mouth/throat irritation (8); nausea/vomiting (7); lachrimation (6); dizziness/faint (4); headache (4), eye irritation (3); lethargy (3); tachycardia (3); anxiety (2). *Conclusion:* All pesticide fumigant exposures in this series involved professional products with exposure frequently occurring subsequent to application, during use by the patient or due to poor storage. Accidental exposures usually produced minor or no symptoms. Where symptoms did occur, respiratory effects were frequently reported. In deliberate self-harm exposures to these products the outcome was often fatal. *References:* 1. Persson HE, Sjoberg GK, Haines JA, et al. Poisoning Severity Score. Grading of acute poisoning. J Toxicol Clin Toxicol 1998; 36:205–13. *Acknowledgement:* The authors appreciate the assistance of the other Units of the NPIS in providing data.

266. Methomyl-Alphamethrin Poisoning Presented with Cholinergic Crisis, Cortical Visual Loss and Delayed Peripheral Neuropathy: A case Report

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Objective: Methomyl-alphamethrin is a combination of carbamate and synthetic pyrethroid insecticides. Carbamates function as cholinesterase inhibitors, which may produce life-threatening cholinergic syndromes that require prompt diagnosis and treatment. Cortical visual loss and peripheral neuropathy have rarely been reported as complications of carbamate or pyrethroid poisoning. Here we report a case of intentional methomyl-alphamethrin ingestion that resulted in coma, respiratory failure, cardiovascular collapse, cortical blindness and delayed peripheral neuropathy. *Case report:* A 41 year-old woman, attempting suicide by drinking 200 mL of methomyl-alphamethrin insecticide, was found unconscious, hypothermic and in shock initially. Spontaneous circulation was resumed after immediate resuscitation and mechanical ventilator support. She became conscious and was weaned from the ventilator on the second day. Clinical diagnosis of carbamate poisoning was confirmed by reduced levels of erythrocyte and plasma cholinesterase, and the presence of methomyl in her urine. On the fourth day after poisoning, she complained of blurred vision. Ophthalmic examinations with electro-retinography and fluorescein angiography were normal. Visual evoked potential showed nearly flat response. Brain magnetic resonance image disclosed abnormal T2 high signal at bilateral basal ganglions and bilateral occipital lobes, indicating the diagnosis of cortical visual loss. At day 21, she noticed lower limb numbness, progressive weakness and right foot drop. Electrophysiological tests at day 27 were consistent with neuropathy of bilateral peroneal nerves. *Conclusion:* This patient sustained severe toxic effects from carbamate poisoning, which was complicated with cortical visual loss and delayed neuropathy, which are seldom mentioned in the literature. Physicians should be aware of these two rare complications in patients with severe carbamate poisoning.

267. Acute Ethylene Chlorohydrin Poisoning: Taiwan Poison Center Study

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Objective: Ethylene chlorohydrin is a chemical that has been used in hastening grape vine sprouting in Taiwan. Although such agricultural use is prohibited, intoxications still occur due to illegal use. Reports concerning human ethylene chlorohydrin poisoning are rare. We report our experience in treating acute ethylene chlorohydrin-poisoned patients. *Methods:* A retrospective study was conducted to evaluate patients with ethylene chlorohydrin exposure reported to the Taiwan Poison Control Center during 1989–2009. *Results:* Thirty-six patients with ethylene chlorohydrin poisoning were identified. There were 24 male and 12 female patients, ranging in age from 2 to 75 years. The intent of exposure was suicidal in 8, unintentional oral in 11, unintentional non-oral in 6, and occupational exposure in 11 patients and their fatality rates were 62.5%, 50.0%, 25.0%, and 16.7% respectively. The severity of poisonings was as follows: fatal 38.9%, severe 11.1%, moderate 11.1%, and mild 38.9%. Most of the fatal cases died on the first day of intoxication. Oral ingestion was the most common route of exposure (55.6%) and the case fatality rate was 55.0% in this group. Dermal exposure involved 25.0% of cases and the case fatality rate was 33.3%. Specific therapy with ethanol or fomepizole was used in 4 and 7 patients, and their fatality rates were 25.0% and 28.6% respectively. *Conclusion:* Acute ethylene chlorohydrin poisoning is an urgent problem. Rapid death can occur after oral or dermal exposure. Experimental data suggest ethanol or fomepizole may be used in such cases, however there were too few patients to reach a definitive conclusion.

268. Deep Coma and Markedly Decreased Blood Pressure After Ingestion of Permethrin and Tetramethrin

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Objective: Ingestion of pyrethroid household insecticides usually shows a benign course. There is little information about blood concentrations in acute poisoning. We present a case of a suicide attempt with permethrin and tetramethrin which resulted in severe intoxication. The ingestion of the product was confirmed by quantification of the primary metabolite of permethrin. *Case report:* A 65 year old woman ingested 250–300 mL of a pesticide containing permethrin, tetramethrin, and piperonyl butoxide dissolved in water and isobutyl alcohol. Half an hour later the paramedics found her awake and normotensive. On admission to the hospital, the patient had deteriorated to deep coma (GCS 4). Her systolic blood pressure was 60 mmHg. Laboratory results revealed a metabolic acidosis (lactate concentration was 8.2 mmol/L). The acidosis worsened despite artificial ventilation and circulatory support with atropine and norepinephrine. Thus hemodialysis was started which resulted in improved consciousness. Nevertheless she had to be ventilated for 3 days because of bilateral aspiration pneumonia. The further course was complicated by ethanol withdrawal. The patient later remembered drinking the pesticide but nothing else. Toxicological analysis of the serum 3.5 hours after ingestion revealed a concentration of 6.4 mg/L of 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid (DCCA). DCCA is formed out of permethrin by ester cleavage *in vivo* and in stored serum. Under the applied conditions all permethrin is expected to be converted to DCCA. This concentration proves a high exposition to permethrin and therefore to tetramethrin too. The latter was only confirmed qualitatively. Blood alcohol was 2.6 g/L (not an ingredient of the product in question). This alcohol level may have contributed to the fast developing coma and marked decrease in blood pressure, even though the patient was used to ethanol. Chronic alcohol ingestion increases the risk of lactic acidosis. *Conclusion:* This is one of the rare cases where ingestion of a pyrethroid containing insecticide resulted in severe toxicity and the ingestion of large amounts of pyrethroids could be proven while there was no evidence for the presence of other pesticides.

269. Acute Pesticide Poisonings in the Years 1994–2008 Reported to the Toxicological Information Centre in Bratislava

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Objective: The National Toxicological Information Centre (NTIC) in Bratislava has frequently been consulted for advice on pesticide exposures. To obtain more information about pesticide poisonings in Slovakia, we performed a retrospective analysis of all telephone calls to our Centre. *Methods:* All telephone inquiries involving pesticide exposures were extracted from our databases for the period 1994–2008. The following data were analysed: age, sex, intent of exposure (accidental or suicidal), substances ingested and clinical severity. All intoxications were classified in accordance with the Poisoning Severity Score. *Results:* During the 15-year period 26,547 acute intoxications were reported to the Slovak NTIC, of which 3,156 (11.9%) involved pesticides. Pesticide exposures in males (60.8%) were more prevalent than those involving females (33.4%). Accidental poisonings were more common (82.5%) than suicidal poisonings (15.8%). Almost half of the cases (48.1%) were children. Most exposures were caused by insecticides (46.0%), but rodenticides (23.3%), fungicides (9.3%), herbicides (12.3%) and other pesticides were also involved. Referring to the insecticides, 39.4% were organophosphates, 36.9% pyrethroids and 8.2% carbamates. Symptoms occurred in 81.2% of patients. The majority of them developed only mild toxicity (63.8%), moderate symptoms occurred in 12.4% and severe symptoms in 4.2% of all poisonings. Twenty-four cases (0.8%) resulted in death. *Conclusion:* Pesticide poisonings are still associated with many fatalities, especially among patients with organophosphate exposures. More efforts,

such as legislative control of the availability of pesticides and further innovation in therapeutic measures, are required to reduce the serious impact of pesticide poisonings.

270. Amitraz Poisoning

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Objective: Amitraz is a formamidine pesticide used as an insecticide and acaricide.[1] In Iran amitraz is mainly used as a pesticide in pistachio plants in the suburbs of Rafsanjan-Iran. Amitraz poisoning causes nausea, vomiting, hypotension, bradycardia, bradypnoea, myosis, mydriasis, hypothermia, drowsiness and coma in humans.[2] *Case series:* The following cases, involving attempted suicide with amitraz intake have been observed in the emergency department of Ali-ebne-abitaleb hospital in Rafsanjan-Iran. Case 1: A 22 year old man was admitted to the emergency department with a history of amitraz ingestion. The patient was initially alert, but had vomiting. The vital signs were stable. However, loss of consciousness occurred later. After endotracheal intubation, he was transferred to ICU. The patient was discharged in good conditions after 4 days. Case 2: A 25 year old man with a history of amitraz poisoning (ingestion) was admitted to the emergency department. He was initially alert but suddenly showed respiratory arrest. Endotracheal intubation was carried out. Mechanical ventilation was employed and the patient was transferred to ICU. Having recovered, the patient was discharged after 5 days. Case 3: A 20 year old woman was admitted to the emergency department with a history of amitraz ingestion. She was alert with normal vital signs, but showed drowsiness and bradycardia. The patient was transferred to ICU and atropine was prescribed. The patient recovered and was discharged after 3 days. *Conclusion:* Loss of consciousness and respiratory depression are important effects of amitraz poisoning. ICU admission and supportive treatment should be considered. *References:* 1. Avsargullaril L, Ikizceli I, Sungur M, et al. Acute amitraz poisoning in adults: clinical features, laboratory findings, and management. Clin Toxicol (Phila) 2006; 44:19–23. 2. Elinav E, Shapira Y, Ofran Y, et al. Near-fatal amitraz intoxication: the overlooked pesticide. Basic Clin Pharmacol Toxicol 2005; 97:185–7.

271. Pesticide Poisoning and its Relation to Pesticide Distribution in Mashhad, Iran

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Objective: Pesticide poisoning is common in Iran.[1] The aim of this study was to investigate the association between patterns of pesticide poisoning and distributed pesticides in Khorasan-razavi, Iran. *Methods:* The 3033 pesticide poisoning cases referred to Imam Reza Hospital in Mashhad, Iran from 2000 to 2008 were evaluated retrospectively. Data on different pesticides allocated to Khorasan-razavi province, Iran were obtained from the Ministry of Agriculture from 1997 to 2008. A poisoning risk index (number of poisonings divided by pesticide distribution/tons ×10) and a mortality risk index (number of deaths divided by pesticide distribution/tons) were calculated. *Results:* Insecticides had the highest distribution rate, varying between 237 and 679.2 tons/year. The lowest distribution rate was for rodenticides, including aluminum phosphide (AP). Two thousand five hundred and seventy eight human insecticide exposures were reported, of which 53.34% were females. The seasonal distribution in insecticide poisoning cases suggested a peak in spring and summer (63.15%). A total of 14 fungicide and herbicide poisoning cases were reported during 2000–2008, of which all fully recovered. Distribution of fungicides and herbicides varied between 225 and 580.2 tons/year. During 2000–2008, 406 cases of rodenticides and AP poisoning were referred to this hospital, having a roughly equal prevalence in females (49.8%) and males; of these a total of 6.4% died. The highest amount of rodenticides and AP allocated to the region was 1.832 tons in 2008. There was a significant ($P<0.01$) relationship between the amount of rodenticides and AP allocated annually and the number of admitted poisoning cases. Poisoning risk indices were 410, 6.5 and 0.04 for rodenticides and AP, insecticides, and fungicides and herbicides, respectively. Mortality risk index was 2.72 for rodenticides and AP and 0.03 for insecticides. *Conclusion:* The number of pesticide poisoning cases increased with the amount of pesticides allocated to the region. Rodenticides and, in particular, aluminum phosphide showed the highest poisoning risk. The seasonal use of insecticides affected the numbers of poisoning cases. *References:* 1. Afshari R, Ghodsi E, Sharifian-Razavi M, et al. Comparison of Pesticide Poisoning in Mashhad (Iran) from 1997 to 2005. Clin Toxicol 2007; 45:382.

272. A Retrospective Case Series of Metam Sodium Poisoning

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Objective: To evaluate the severity and toxicity of poisoning by metam sodium, a dithiocarbamate fumigant, the breakdown products in soil of which are methylisothiocyanate (MITC), carbon disulfide (CS_2) and hydrogen sulfide (H_2S).[1] *Case series:* A retrospective review of 102 cases of metam sodium exposure reported to the Poisons and Toxicovigilance Center (CAPTV) between 1992 and 2009. *Results:* All cases of exposure were unintentional. Occupational poisoning only occurred in eight cases. The most common route of exposure was inhalation (n = 96). In 79 cases, the patients were people living near fields where metam sodium had recently been applied. Most of the reported symptoms involved irritation of the eyes (n = 76), throat and nose (n = 65), attributable to MITC. Cough and dyspnea occurred in four cases but no persistent, irritant-induced asthma or persistent exacerbation of asthma was observed. Sixteen patients at two different sites of pollution were exposed via the sanitation systems in their homes following the illicit discharge of metam sodium into the sewers. Most presented with nausea and headaches but only four experienced eye or throat irritation. We hypothesized that a breakdown product other than MITC was involved, and air analysis at one site revealed the presence of CS_2 (337 mg/m^3) and no H_2S. Two of these patients, who had consumed some alcohol, experienced dysgeusia but no disulfiram-like reaction. The only lethal case recorded was a truck driver who was found dead of acute lung injury after falling into a tank that had previously contained metam sodium. Two other patients who ingested a dilute solution presented mild epigastric pain. Four skin exposures caused erythema (n = 2), moderate burns (n = 1) and urticaria (n = 1). Seventy per cent of all affected patients underwent a medical assessment. According to the poisoning severity score, their symptoms were minor in 99% of cases. *Conclusion:* Acute metam sodium exposure usually causes minor symptoms. Nevertheless, the toxicity of its breakdown products can cause severe symptoms in a stuffy environment. An air analysis of MITC, CS_2 or H_2S may be recommended in such cases. *References:* 1. Cone JE, Wugofski L, Balmes JR, et al. Persistent respiratory health effects after a metam sodium pesticide spill. Chest 1994; 106:500–8.

273. Multicentre Data Collection on Paraquat Poisoning in Europe

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Objective: Paraquat has been used as a herbicide worldwide since 1962. The aim of this study was to collect adverse health incident data to a common standard in Europe, using paraquat as model substance. *Methods:* Poisons Centre-based prospective multicentre cohort study in 9 European countries where paraquat was marketed during 2006–2008. In the first months of 2006 data were collected in a retrospective pilot study. Patient and exposure characteristics were recorded and likelihood of exposure, symptoms, severity, causality, and outcome were assessed. Only cases with a high likelihood of exposure are analyzed here. *Results:* Total reported cases n = 419 (Greece 97, Spain 93, Portugal 84, United Kingdom 60, France 38, Italy 17, Belgium 6, Germany 12, Netherlands 8, Slovakia 3, Cyprus 1). Three hundred and eleven (74%) had a high likelihood of exposure. Patient characteristics: Adults n = 292, mean age 52.0 years (S.D. 18.2, range 16–92), children (age <16 years) n = 16, mean age 7.5 years (S.D. 4.5, range 1.0–15), unknown n = 3. Severity and outcome according to circumstances of exposure are listed in Table 1. The route of exposure was oral in 161, dermal 62, inhalation 38, ocular 12, mucosal 2, combined 36. Paraquat could be analytically detected in 84 cases (52.5% of all cases tested). Symptoms were mainly gastrointestinal, pulmonary, renal (from oral ingestion), and dermal. *Conclusion:* Paraquat poisoning is particularly prevalent in Southern Europe. Severe or fatal poisoning is more frequent in intentional than in accidental/occupational exposure (Chi^2 $p<0.0001$). There was no fatal case and only two severe occupational cases.

274. Tolerance to Morphine-Induced Respiratory Effects in Mice: Description and Mechanisms

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Objective: Morphine is responsible for severe poisonings. Morphine toxicity may be attributed, in chronically treated patients, to the development of a weaker tolerance for its respiratory effects in comparison to its analgesic effects. Our objective was to describe the tolerance to the respiratory effects of morphine in mice and to investigate its mechanism. *Methods:* Experimental study in Swiss mice with intraperitoneal administration of 2.5 mg/kg/day morphine versus saline; description of the respiratory effects (using plethysmography under

Table 1. Severity and outcome according to circumstances of exposure

Severity	occupational	accidental	intentional	unknown	total
asymptomatic	11	21	5	1	38
minor	55	45	20	2	122
moderate	11	11	13	2	37
severe	2	2	14	4	22
fatal	0	5	68	2	75
unknown	5	2	6	4	17
Total	84	86	126	15	311

4%-FiCO$_2$, N = 10/group); calculation of the 50%-effective dose (ED50); *in vitro* study of 3H-DAMGO binding on 2 brain structures (periaqueductal grey region [PGR] and brainstem); *in vitro* measurement of adenylate cyclase activity after amplification using forskoline and stimulation of mu-opioid receptors with DAMGO; comparisons using ANOVA for repeated measurements followed by Bonferroni post-test. *Results:* The tested analgesic dose of morphine was responsible for significant respiratory effects characterized by a significant increase in inspiratory time. Repetitive administration of 2.5 mg/kg/day morphine during 10 days induced a 2-fold increase in the ED50 if determined in air and a 4-fold increase in CO_2. In the brainstem, DAMGO induced a moderate inhibition of AMPc production in mice treated with morphine, although with a trend towards a stronger inhibition in comparison to controls. In PGR, an overstimulation of AMPc production in response to DAMGO was observed, significantly more important in morphine-treated mice than controls ($p < 0.05$). In contrast, no significant differences in mu-opioid receptor-associated adenylate cyclase activity between the PGR and brainstem were observed. Similarly, no significant modification in membrane expression of mu-opioid receptors based on differences in 3H-DAMGO binding was observed between both regions. *Conclusion:* Analgesic doses of morphine are responsible for significant increase in inspiratory time. Tolerance to morphine respiratory effects remains limited at day 10 of a repeated administration, in comparison to the tolerance to its analgesic effects (previously determined in our laboratory as a 13-fold increase in ED50). This difference in tolerance can be related neither to a difference in the receptor expression on membranes nor to an alteration in adenylate cylcase activity. Involvement of other anti-opioid neurotransmitters (including cholecystokinine, dopamine, serotonin or glutamate) should be hypothesised.

275. Mechanisms of High-Dose Citalopram-induced Death In Rats

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Objective: Citalopram is a selective serotonin reuptake inhibitor. Citalopram toxicity is considered as weak. However, overdoses may result in serotonin syndrome, seizures, electrocardiographic abnormalities as well as respiratory failure and death. Mechanisms of severe toxicity remain unclear. Our objective was to study the mechanisms of death following high-dose citalopram administration in rats. *Methods:* Experimental study in Sprague Dawley rats with intraperitoneal (IP) citalopram administration; determination of the median lethal dose (MLD) using the Dixon & Bruce up-and-down method; clinical descriptive study of citalopram-induced features and measurement of alterations in respiratory pattern (arterial blood gases and plethysmography) and biological parameters including blood lactate (Scout®, EKF diagnostic), plasma and platelet serotonin concentrations (high-liquid performance chromatography - fluorometry); determination of the preventative activity on seizures and death of diazepam, cyproheptadine, and propranolol pretreatments with the determination of their minimal effective dose; comparisons using ANOVA for repeated measurements followed by Bonferroni post-test. *Results:* Citalopram IP-MLD was determined as 102 mg/kg in rats. Seizures were significantly increased in rats receiving 80% and 120% of citalopram MLD versus controls ($p<0.01$ and $p<0.05$, respectively), while death rate was only significantly increased in rats treated with 120% of citalopram MLD ($p<0.001$). Significant decrease in body temperature was observed after 90 minutes in rats treated with doses >60% MLD in comparison to controls ($p<0.05$). Occurrence of serotonin behavioural syndrome was comparable in all groups. Citalopram administration did not result in significant hypoxemia, hypercapnia, and lactate elevation, thus not supporting the hypothesis of the occurrence of any significant deleterious cardiovascular effect in citalopram-induced toxicity. However, a significant moderate increase in the inspiratory time ($p<0.05$) accompanied with an expiratory braking was observed. A significant decrease in platelet serotonin and increase in plasma serotonin concentrations were measured ($p<0.05$). Pre-treatment with diazepam (1.77 mg/kg) and cyproheptadine (17.1 mg/kg) of rats receiving a lethal citalopram dose prevented seizures and death, while propranolol was ineffective. *Conclusion:* Citalopram respiratory toxicity remains mild, while deaths resulting from seizures are probably related to serotonin toxicity. Our observations may be helpful to better understand and manage human citalopram poisonings.

276. UK Trends in Toxicity Relating to Drugs of Misuse from National Poisons Information Service Data

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Objective: Toxicity relating to drugs of misuse is a common reason for presentation to hospital. Health professionals are likely to seek advice about management from a poisons centre, especially when they are unfamiliar with the agent involved or toxicity is severe. Poisons centre data may therefore be useful in tracking acute harms relating to drugs of misuse. This study was therefore performed to examine trends in NPIS enquiries for drugs of misuse and compare this with other sources. *Methods:* National study of telephone enquiries (2002–2009) and TOXBASE® accesses (2000–2009) relating to drugs of misuse. Since total TOXBASE® accesses have increased substantially and telephone enquiries have decreased for all products over the course of the study, data are presented as percentages of overall telephone or TOXBASE® activity for each year studied. *Results:* Ecstasy was the most common drug of misuse accessed on TOXBASE® or subject to a telephone enquiry during the study, but the proportion of activity relating to this drug declined for both telephone enquiries (2002 0.85%, 2008/9 0.38%) and TOXBASE® accesses (2000 1.36%, 2008/9 0.72%). In contrast, over the same time periods the proportion of telephone (0.37% to 0.59%) and TOXBASE® activity (0.28% to 0.71%) relating to cocaine has increased markedly. Cocaine is now the most common drug of misuse involved in telephone enquiries and the second most commonly accessed from TOXBASE®. Although less commonly encountered, increases in the proportion of telephone and TOXBASE® activity have also been observed for methamphetamine (telephone 0.002% to 0.025%; TOXBASE®, 0.008% to 0.025%) and benzylpiperazine (telephone 0% to 0.056%; TOXBASE®, 0.002% [for 2005/6, the first year that information was available for access] to 0.56% in 2008/9). *Conclusion:* Increases in the proportion of NPIS activity relating to cocaine are consistent with national statistics and other studies[1] reporting increased prevalence of use, arrests, drug seizures and deaths relating to the drug. NPIS data appear useful for following trends in toxicity relating to drugs of misuse. *Reference:* 1. Schifano F, Corkery J. Cocaine/crack cocaine consumption, treatment demand, seizures, related offences, prices, average purity levels and deaths in the UK 1990–2004. J Psychopharmacol 2008; 22:71–9.

277. Takotsubo Cardiomyopathy Associated with Cocaine Intoxication

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Objective: Takotsubo Cardiomyopathy (Apical Ballooning Syndrome) is an acute, transient left ventricular dysfunction synonymous with myocardial stunning associated with severe emotional distress ("broken heart syndrome") suggested linked to catecholamine toxicity.[1] We observed a patient with profound hypotension following cocaine use. An echocardiogram revealed the apical ballooning syndrome and global systolic dysfunction. We report this case to further support the potential association with cocaine use and the need for clinical vigilance in diagnosing and treating this syndrome. *Case report:* A 42 year old female presented to our Emergency Department (ED) complaining of weakness and abdominal pain, which began hours after a several day cocaine binge. Physical examination revealed lethargy, hypotension (BP 80/60 mmHg), pallor, jugular venous distension, clear lungs, and epigastric tenderness. Initial labs were notable for a white blood cell count of 17.2 Thous/uL, compensated metabolic acidosis with a lactate of 1.8 mmol/L and hemoglobin of 11.2 g/dL. EKG showed sinus bradycardia without acute ST segment changes. A urine drug screen confirmed cocaine use. Despite aggressive fluid resuscitation in the ED, her systolic pressure declined to 40 mmHg and her mental status worsened. Her abdomen became increasingly tender; bedside ultrasound showed fluid in Morrison's pouch and the splenorenal area. She was intubated, transfused blood and underwent an exploratory laparotomy. With persistent hypotension after a negative exploration (300 cc ascites secondary to fluid resuscitation), an emergent transthoracic echocardiogram revealed akinesis of the anterior, septal, lateral and inferior walls from mid-wall to the apex with only the basal segments contracting normally and severe global systolic dysfunction with an LVEF of 30%. She improved with fluids and dobutamine; repeat transthoracic echocardiogram on day 4 demonstrated improved LV function. *Conclusion:* This case describes cardiogenic shock secondary to Takotsubo cardiomyopathy in the setting of heavy cocaine use. We report this case to support the theory of a catecholamine mediated mechanism and potential association with cocaine use. Clinicians should consider this diagnosis in patients with hypotension and cocaine use. *References:* Wittstein IS, Thiemann DR, Lima JAC, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. NEJM 2005; 352:539–48.

278. Acute Ethanol Poisoning - Epidemiological Study in a Period of Nine Years

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Background: Acute ethanol poisoning and the consequences associated with severe alcohol consumption are the most common causes of hospitalization in many countries, affecting all age groups, both genders and almost all social groups. *Objective:* To assess the frequency of acute ethanol poisoning among patients admitted to the Clinic of Toxicology, Emergency Hospital "N.I.Pirogov" from 2000 to 2008 and to analyze some epidemiological data - distribution, dynamics, trends. *Methods:* The records of the Toxicology Clinic, Emergency Hospital "N. I. Pirogov" were reviewed retrospectively for all ethanol poisonings during the period from January 1, 2000 to December 31, 2008. The patient's age and gender were recorded. *Results:* Data of 3828 patients intoxicated by ethanol were analyzed, aged from 15 to over 35 years. Monotoxic ethanol acute poisoning was registered in 3280 of these patients and mixed (ethanol and other psychoactive drug or various toxic agents) acute poisoning was registered in 548 persons. From the period of 2000 to 2008 the consumption of alcohol increased two-fold. The frequency of monotoxic ethanol poisoning was highest during 2007 and the frequency of mixed poisoning - in 2001. Male prevailed over the female (ratio - 3:1) in persons with monotoxic ethanol poisoning. The relationship male to female was 1:1 in persons with mixed poisoning. Acute alcohol intoxications ware the most common among the people over 35 years old, following by adolescents under 15 years. *Conclusion:* The results demonstrate that the consumption of ethanol was increasing during the studied period. The percent-

age of those intoxicated with ethanol was higher among men and patients over 35 years old and adolescents under 15 years, a fact that is extremely disturbing. Our results show the value of epidemiological investigations for planning prevention programs and the need for such programs among adolescents to prevent excess drinking and the numerous health problems associated with it.

279. MDPV Exposures Reported to the Finnish Poison Information Centre

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Objective: The designer drug MDPV (also known as MDPK or 3,4-methylenedioxypyrovalerone) was first reported to EMCDDA (European Monitoring Centre for Drugs and Drug Addiction) in December 2008 by Finland. MDPV is regulated as illegal to sell or possess in some countries. In Finland it is considered as a medicine and a chemical and import is forbidden, but it is bought via the Internet. MDPV is a psychoactive drug acting by releasing and inhibiting the reuptake of monoamine neurotransmitters such as dopamine and norepinephrine. Its CNS stimulant effects are cocaine- and amphetamine- like. It is also considered to have aphrodisiac properties. The effects seem to be stronger than those of a comparable amount of amphetamine. Duration of the effect has been reported to be 3 - 6 hours. Information on overdoses is scarce in the scientific literature. We investigated the human MDPV exposures in calls to the Finnish Poison Information Centre (PIC) to gain some information on the clinical picture of MDPV overdoses. *Case series:* In Jan 2008 - Oct 2009, the Finnish PIC received in total 33 calls concerning MDPV exposures. It was used intranasally, orally (PO), rectally or intravenously (IV). Doses used were 10 mg (up to 30 mg) PO and 5 mg IV. Five of the patients, aged 21–31 years, needed hospitalisation. All of them had tachycardia, agitation, dyspnoea and hypertension. Two patients had reduced level of consciousness; one of them had convulsions and needed intubation for 1/2 day. *Conclusion:* MDPV seemed to cause mostly tachycardia, dyspnoea, hypertension, and agitation. Disturbed consciousness was observed in 2 cases.

280. The Comparative Clinical Effects of Cocaine and Amphetamines

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Objective: Cocaine and amphetamines are indirectly acting sympathomimetic drugs. They differ, however, with regard to mechanisms of action, commonly used routes of use, and associated complications. Patients exhibiting acute toxicity by either agent may present similarly. The objective of this study is to compare differences between these agents for various adverse clinical effects in cases reported to a statewide poison network. *Methods:* We analyzed the clinical effects of acute cocaine or amphetamines exposures, with no other known concurrent drug intoxications, in surviving patients reported to a large poison center network. The cohort examined consisted of 2149 patients presenting between 2002 and 2005. The relative risk of various adverse outcomes was compared. *Results:* Most reported clinical adverse effects were similar between the two agents. Only those that were significantly different are shown in Table 1, all of which were more severe for amphetamine cases. *Conclusion:* In this study, increased adverse clinical effects associated with muscle injury and associated rhabdomyolysis and subsequent renal failure were more highly associated with amphetamine intoxication than with cocaine intoxication. This may be due to the longer duration of action of amphetamines relative to cocaine or other still yet to be defined mechanisms. Larger prospective studies are needed to better evaluate this possible association.

281. Ketamine Abuse Related Illnesses: A Rapidly Emerging Problem in Taiwan

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Objective: Ketamine abuse is a rapidly emerging problem in Taiwan. Consequently, ketamine related illnesses (e.g. interstitial cystitis) are more frequently encountered in daily practice; the pattern and outcome of such events however remain unclear. We conducted a hospital-based study to understand the clinical profiles of patients who sought medical care because of ketamine related illnesses. *Methods:* We identified patients from two different sources: (1) patients who visited the emergency department (ED) of Taipei Veterans General Hospital (TVGH) because of ketamine related illnesses and whose urine was tested positive for ketamine between 2000 and 2008; (2) patients hospitalized to TVGH because of ketamine related interstitial cystitis during the same period. All patients' data were then collected and analyzed by employing appropriate statistical methods. *Results:* Between 2000 and 2008, there were a total of 127 patients eligible for the study, including 114 ED patients with a positive urine test for ketamine, and 13 patients who were hospitalized because of clinically diagnosed ketamine related interstitial cystitis. The number of patients with ketamine related illness increased rapidly by time from 2000 through 2008. In addition, the rising trend was positively correlated with the annual amount of seized ketamine during the study period (r = 0.729). Ketamine related illnesses mainly involved people of younger age, unmarried status, and high school education. Most patients sought medical care because of illnesses other than acute poisoning, and common manifestations included neurological symptoms (26.8%), psychiatric symptoms (23.2%), and genitourinary tract symptoms (16.5%). Seventy-nine patients were hospitalized; three patients (2.4%) died and 52 patients (40.9%) developed sequelae. *Conclusion:* The number of ketamine abusers and related illnesses is rapidly increasing in Taiwan. Many patients with ketamine related illness sought medical care through ED. Because quite a few ketamine abusers developed serious sequelae, it is mandatory to refine the national drug control policy and relevant preventive strategies to effectively minimize the impact of ketamine related health hazards in Taiwan.

Table 1. Significantly different clinical effects: amphetamines (AMP) vs. cocaine (COC)

Clinical effects	AMP	% Total	COC	% Total	Ratio	95% CI
Hypotension	5	4.5	21	1.0	4.57	1.35–12.45
Tachycardia	38	33.9	470	21.9	1.55	1.08–2.16
CPK elevation	7	6.3	29	1.3	4.63	1.71–10.81
Neurological (any)	62	55.4	737	34.3	1.61	1.23–2.09
Agitation, irritability	43	38.4	370	17.2	2.23	1.59–3.06
Confusion	10	8.9	84	3.9	2.28	1.06–4.41
Hallucinations, delusions	12	10.7	32	1.5	7.20	3.38–14.35
Oliguria, anuria	3	2.7	2	0.1	28.78	3.30–344.59
Renal failure	2	1.8	3	0.1	12.79	1.07–111.67

282. Mephedrone - A New 'Legal' Online Drug of Abuse. Do we Know Anything About its Safety?

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Objective: The UK NPIS are receiving an increasing number of calls about a drug of abuse known as mephedrone or 4-methylmethcathinone, also called 'bubbles'. It is usually supplied as an off-white crystalline powder with a strong fish-like odour and is either ingested or inhaled. This drug is becoming increasingly popular in the UK as it is currently classed as a legal substance. It is often bought from the Internet as plant food or as a research chemical marked 'not for human consumption.' *Methods:* Enquiries to the UK NPIS for the period 1 January 2008 to 1st January 2009 and also 1st January 2009 to 1st November 2009 involving 'mephedrone' or 'methcathinone' were retrieved. Each call was examined in detail and all reported symptoms and the results of any investigations noted. Internet websites were also investigated for details of mephedrone exposures to try and compare symptoms experienced by regular users with those reported to the UK NPIS. *Results:* No enquiries concerning mephedrone were received by UK NPIS between 1st January 2008 and 1st January 2009 compared with 29 enquiries which were received between 1st January 2009 and 1st November 2009. Of these, the main symptoms reported were agitation/anxiety, headache, sweating, chest pain, mydriasis, loin or back pain and pins and needles. One patient was admitted to ITU with tachycardia, hypotension, rhabdomyolysis and coma following a seizure. The symptoms reported on the Internet (from 13 user information reports) included euphoria, addictive behaviour, dilated pupils, jaw clenching and sweating as well as increased heart rate. There have been some reports of vasoconstriction causing purple extremities and joints. One death has been reported in Sweden although causal links with mephedrone have not yet been confirmed. *Conclusion:* Mephedrone is a very new and increasingly popular drug; its legal status in the UK may falsely imply safety. It is, however, a synthetic drug that, from UK NPIS data and Internet reports, causes some potentially dangerous symptoms that are similar to stimulant drugs of abuse. The clinical effects of this chemical need further investigation.

283. A Study Assessing Representation in Patients Presenting to the Emergency Department with Acute Recreational Drug Toxicity

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Objective: Acute recreational drug toxicity is a common reason for presentation to the Emergency Department (ED). Previous studies have shown that a significant proportion of those (up to 27%) who present with acute recreational drug toxicity in a pre-hospital (nightclub) environment, have previously presented with toxicity with similar drugs.[1] There is no published data looking at representations to the ED following an initial ED presentation with acute recreational drug toxicity. *Methods:* We retrospectively identified patients presenting with acute recreational drug toxicity during 2007; the first presentation was used as the "primary presentation". We then determined whether there had been any further acute poisoning ED presentations between this presentation and 31st August 2009 and determined: i) mean (SD) number of representations; ii) time to second presentation; iii) concordance of drugs used at primary and second presentations; iv) number of representations due to deliberate self-poisoning. *Results:* There were 446 "primary presentations" during 2007; of these 44 (9.9%) individuals had ≥1 acute poisoning representation before 31st August 2009. The mean±SD (range) number of representations and time to first representation was 1.34±0.68 (1–4) and 257.5 ± 229.6 (2–680) days respectively. 86.4% of first representations were related to acute recreational drug use, with 89.5% concordance of drugs used. Overall, there

were 8 (1.8% of all individuals) self-poisoning representations (mean±SD (range) time to self-poisoning presentation 267.8±213.4 (21–702) days). *Conclusion:* A small, but clinically significant, minority of individuals represented with acute recreational drug toxicity; in the majority of these the same drug(s) were responsible for the representation. There is the potential for brief interventions in the ED for patients with acute recreational drug toxicity to try and prevent future presentations. Further work is needed to develop the brief intervention tools and identify the potential target group(s) for these interventions. Although only a small proportion of representations relate to deliberate self-poisoning, this is greater than in the normal population and clinicians need to be aware of the potential for subsequent self-harm in those with acute recreational drug toxicity. *References:* 1. Wood DM, Nicolaou M, Dargan PI. Epidemiology and aetiology of recreational drug toxicity in a nightclub environment. Subst Use Misuse 2009; 44:1495–502.

284. Hypotension and Syncope After Recreational use of Viagra™ and Rush (Isobutyl Nitrite): an Opportunity for Targeted Education

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Objective: Sildenafil, marketed as Viagra™, is used to treat erectile dysfunction. Since sildenafil was introduced epidemiologic reviews have documented use along with drugs of abuse including: cocaine, amphetamine and amphetamine derivatives such as MDMA as well as 'poppers' which are volatile nitrate or nitrite compounds. Sildenafil use with cocaine or amphetamine is often in the setting of transient drug-induced erectile dysfunction whereas sildenafil use with 'poppers' is for purported effects on orgasmic pleasure. We report a case of syncope and hypotension associated with sildenafil and isobutyl nitrite use and review the literature regarding recreational Viagra™ or other phosphodiesterase inhibitor use. With additional information certain groups at risk for sequelae related to high-risk behaviors may be targeted for harm reduction and educational strategies. *Case report:* A 62-year-old male was found unconscious in an adult bookstore. He had sustained a facial laceration after apparently 'passing out' in the back of the store. Paramedics documented an initial blood pressure of 70/palpable and heart rate of 88 beats-minute. Repeat BP was 72/48 on arrival at the Emergency Department. The patient described ingesting sildenafil earlier in the evening in anticipation of a sexual encounter. He had then used Rush by inhaling it from under his nose after which he 'passed out'. After 1 liter of saline his blood pressure improved to 90/60 mmHg. An EKG demonstrated normal sinus rhythm. The patient had no recrudescence of symptoms and his blood pressure remained >90 mmHg after the intravenous fluid. *Conclusion:* Use of nitrates is contraindicated concomitantly with sildenafil over concern for hypotension. Isobutyl nitrite is a novel source of nitrite that is used for facilitating smooth muscle relaxation during sexual intercourse and for its purported enhancement of the effects of orgasm. Although adverse effects could be predicted based on an understanding of the individual chemicals mechanism of action this is the first reported case of syncope due to hypotension from the concomitant use of sildenafil and isobutyl nitrite. This type of drug use is illustrative of a particular intent in drug use and certain demographics may be targeted for education and harm reduction strategies regarding safe sex and recreational drug use.

285. The Effect of Prehospital Naloxone Administration on Vital Signs

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Background: Naloxone is frequently used by prehospital care providers to treat suspected heroin and opioid overdoses. One of the most feared complications from its use is the development of noncardiogenic pulmonary edema. This entity is thought to be due to sudden changes in pulmonary pressures manifest by acute vital sign changes after naloxone administration. However, previous studies have poorly documented vital sign changes after naloxone administration. *Objective:* The objective of this study is to assess vital sign change with the prehospital administration of naloxone. *Methods:* A retrospective study design was utilized. All prehospital patients during a 30 month period presenting to a large suburban teaching hospital were reviewed for the administration of naloxone. Data collected included patient characteristics, initial vital signs, initial oxygen saturation (by pulse oximeter), initial Glasgow Coma Scale, post-naloxone vital signs, post-naloxone oxygen saturation and post-naloxone Glasgow Coma Scale. Pre and post-naloxone vital signs and Glasgow Coma Scale were compared using paired Student's T test. A $p < 0.05$ was considered significant. This study was approved by the hospital and state Institutional Research Board. *Results:* 293 patients were identified and included in this study. Fifty-four percent were male with an average age of 51 years. There were statistically significant increases in oxygen saturation (91 vs 95%, $p<0.0001$) and Glasgow Coma Scale (7.2 to 9.4, $p<0.0001$) were found. No significant changes were found in the systolic or diastolic blood pressure or heart rate. *Conclusion:* Naloxone usage prehospitally has minimal effects on blood pressure and heart rate while improving oxygen saturation and level of consciousness. These findings do not support the theory of sudden autonomic system effects causing opioid induced noncardiogenic pulmonary edema.

286. Evaluation of Opium and Ethanol Level in Fatal Vehicle Accidents

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Objective: Nowadays motor vehicle accidents are one of the commonest accidents, with high mortality and morbidity rates. Due to resulting disability and the need for various diagnostic and therapeutic methods, these inflict great economic loss on society. Alcohol and illicit drug abuse and their side effects are among the most important underlying reasons for such accidents especially in western countries. Due to safety precaution (seat belt and helmet) misuse, law disobedience, speeding, and slow driver's reaction in alcohol related accidents the consequences are graver and the mortality rates higher. *Methods:* In this series of 105 cases, those who died in motor vehicle accidents were tested for vitreous alcohol levels and illicit drugs in the gall bladder. *Results:* 8.6% of these had positive alcohol test results and 42.9% had positive gall bladder illicit drug test results. In this series a strong relationship between sex and education of the deceased and alcohol and opium usage was not found. However, there was such a relationship between age of the deceased and alcohol and opium abuse. Also we found the same relationship between alcohol and opium abuse and the days of the week. *Conclusion:* According to the rampancy of alcohol and illicit drug abuse in fatal accidents, periodic opium tests and random alcohol tests on roads may be effective in reducing accidents and mortality rates.

287. The Prevalence of Websites Promoting the Recreational use of *Datura* or its Sale: A Case Report and Analysis of the Danger to Public Health

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Objective: Plants of the genus *Datura* contain tropane alkaloids with significant anticholinergic activity in humans. Recreational use of *Datura* to deliberately induce an anticholinergic delirium is not uncommon. We recently saw a case of altered mental status in a 22-year old man following the ingestion of vodka and seeds of *Datura stramonium*. After his acute intoxication resolved, the patient reported that he learned about the recreational use of *Datura* on the Internet and subsequently purchased *Datura stramonium* seeds from an online vendor. We investigate the availability of both information about *Datura* and seeds for purchase on the Internet and discuss the wider implications of layperson use of the Internet for information on recreational substance use. *Methods:* Using the English, French, Spanish, and German language Google search engines, we conducted a search in each language of two to three *Datura*-related search terms and reviewed the first 200 search results for websites with unique domain names recommending the recreational use of *Datura* or selling seeds of genus *Datura*. *Results:* The results are summarized in Table 1. *Conclusion:* Anticholinergic toxicity following recreational use of *Datura* remains an important international public health issue. Websites recommending the recreational use of *Datura* are prevalent in German, French, Spanish, and English languages. Additionally, seeds are easily available for purchase from website vendors in each of the above languages. A continuing public health effort to educate laypersons of the danger of obtaining information on the Internet on the recreational use of both licit and illicit substances, including *Datura*, needs to be maintained.

288. Development of a Protocol for the Management of Acute Gamma-hydroxybutyrate and Gamma-butyrolactone Withdrawal

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Objective: Gamma-hydroxybutyrate (GHB) and gamma-butyrolactone (GBL) are commonly used recreational drugs. There have been reports of GHB/GBL dependency predominately from the USA, with a severe withdrawal syndrome on sudden cessation of use.[1]

Table 1. Availability of *Datura* on the Internet using Google

Language & Google search engine	Search terms used	# of websites recommending recreational use of *Datura*	# of vendors selling *Datura* seeds	# of websites both recommending recreational use of *Datura* and selling *Datura* seeds
English - http://www.google.com	*Datura*, jimson weed, *Datura* seeds	15	14	1
French -http://www.google.fr	*Datura*, stramoine, graines *Datura*	12	22	1
German - http://www.google.de	*Datura*, stechapfel, *Datura* samen	11	34	0
Spanish - http://www.google.es	*Datura*, estramonio, toloache, semillas *Datura*	14	14	3

There is no clear management algorithm for patients with GHB/GBL withdrawal. *Methods:* Patients with acute GHB or GBL withdrawal were identified retrospectively (May 2008 to October 2009). Data was extracted from ED and/or medical notes on frequency of GHB/GBL use, presenting clinical features, treatment (including need for admission to a critical care facility) and outcome. *Results:* There were 11 (10; 90.9% males) presentations with acute GHB/GBL withdrawal (GBL-6, GHB-5, Unknown-1); the mean (SD) age was 28.7±4.0 years. Two presented initially with GBL overdose, with subsequent withdrawal; the remaining all had acute features of withdrawal on presentation (agitation, tachycardia, anxiety, hypertension, hallucinations, paranoia). All had a history of GHB/GBL use on multiple occasions throughout the day. Three patients were discharged from the ED with a mean (SD) observation period of 4.2±2.6 hours, single dose benzodiazepine treatment was required in two. Of the 8 presentations admitted to hospital, four (50%) were admitted to critical care (HDU/ITU). Initial treatment was predominately with high-dose benzodiazepines (mean (SD) diazepam equivalent in first 24 hours was 114.4±61.2 mg), with one patient treated with barbiturates as they were already on ITU for GBL overdose. The first four presentations were treated throughout their admission with as required benzodiazepines (diazepam/lorazepam). We then introduced a management plan: patients were treated with as required benzodiazepines in the first 24 hours, and then withdrawn using a high-dose chlordiazepoxide alcohol withdrawal regimen. All patients were discharged from hospital following appropriate withdrawal with no short-term sequelae, and there were no treatment-related adverse outcomes. *Conclusion:* These cases highlight that GHB/GBL withdrawal can be associated with severe clinical features, with high-dose benzodiazepine requirements in the first 24 hours and a significant proportion requiring ITU admission. It appears that the use of chlordiazepoxide-based alcohol withdrawal regimen is appropriate and safe after an initial 24 hours of as required benzodiazepines. *References:* 1. Wojtowicz JM, Yarema MC, Wax PM. Withdrawal from gamma-hydroxbutyrate, 1,4-butanediol and gamma-butyrolactone: a case report and systematic review. CJEM 2008; 10:69–74.

289. Hepatitis C, Hepatitis B and HIV Infections in Intravenous Drug Users in Greece and Associated Risk Behavior

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Objective: To evaluate variation in the rate of infectious diseases in intravenous substance users in Greece during the last 5 years and to highlight risk behavior associated with infection. *Methods:* We studied a cross-sectional sample of drug users in Greece, from 2004 to 2009. The subjects were admissions to the Addiction Department "Ianos" of the Psychiatric Hospital in Thessaloniki, Greece, which is a residential facility running a 21 day detoxification program providing support and preparation for transfer to further treatment. We recorded the gender, age, education level, presence of infectious disease and associated risk behavior. Correlation of Hepatitis C (HCV), Hepatitis B (HBsAg), and HIV infection with risk behavior and education level was assessed with univariate and multivariate regression analysis. *Results:* HCV infection was encountered in 38% of individuals admitted in 2004 and showed a slight decline until 2009 when 36% of admissions were tested positive. HBsAg infection rate was very low (<1%) and HIV infection was not recorded in our admissions during the last 5 years. HCV infection was associated with needle sharing, injecting drugs for more than 2 years, not using a condom and low education level. Multivariate regression analysis showed that needle sharing and injecting drugs for more than 2 years were independently associated with HCV infection. *Conclusion:* HCV infection showed a slight decline across the years studied. The fact that none of our admissions presented with an HIV infection does not reflect the real situation in Greece, but implies that HIV positive users prefer substitution programs. Nevertheless, HIV rate in Greece on a national level is reported surprisingly low compared to other countries,[1] but this could be due to inadequate surveillance.[2] *References:* 1. Mathers BM, Degenhardt L, Phillips B, et al. 2007 Reference Group to the UN on HIV and Injecting Drug Use. Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review. Lancet 2008; 372:1733–45. 2. Reintjes R, Wiessing L. 2nd-generation HIV surveillance and injecting drug use: uncovering the epidemiological ice-berg. Int J Public Health 2007; 52:166–72.

290. Mephedrone: A Novel Synthetic Cathinone - a Case Series of Sympathomimetic Toxicity Associated with its Use

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Objective: Cathinone is an active alkaloid extracted from the leaves of the Khat plant (*Catha edulis*). Mephedrone (4-methylmethcathinone, 4-MMC), a synthetic derivative of cathinone, has recently been reported as a novel recreational drug.[1] There is little published on the toxicity associated with mephedrone. *Methods:* We retrospectively identified patients presenting to our large inner-city Emergency Department (ED) following the use of mephedrone from 1st January 2008. Data was extracted on any co-used substances, clinical features on presentation to the ED, treatment(s) required and outcome. *Results:* 11 patients (8; 72.7% male) were identified, all presenting in 2009, with a mean (SD) age of 26.9±6.8years. Baseline clinical features are in shown in Table 1. Four patients had used mephedrone with ethanol alone and five had used GHB/GBL with the mephedrone; other co-used drugs included cocaine, opium, ketamine and methylone (MDMC). Sympathomimetic features settled within 12 hours of presentation to the ED in all of the patients; four (36.4%) patients required treatment with oral benzodiazepines (lorazepam/diazepam) in addition to symptomatic care. All patients were discharged home with no long term sequelae and no mephedrone related complications. *Conclusion:* This is the first case series reported of toxicity associated with the use of mephedrone (4-MMC). Clinical features of sympathomimetic toxicity in these patients appeared to be short-lived. More data is needed on toxicity associated with mephedrone and other cathinonines to ensure appropriate control. *References:* 1. Wood DM et al. Recreational use of Mephedrone (4-methylmethcathinone, 4-MMC) with associated sympathomimetic toxicity. J Med Toxicol 2009; In press.

291. JWH-018, JWH-073, and Spice

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Objective: To describe an inhaled exposure to Spice, and discuss the synthetic cannabinoids JWH-018 and JWH-073. *Case report:* A 16 year old female presented with altered mental status. The patient became agitated and tachycardic after smoking a product known as Spice. Other vital signs and physical exam findings were normal. After supportive care, the patient was discharged to home without complications. Spice is a mixture of plant matter that is typically smoked for recreational purposes.[1] Spice contains multiple psychoactive compounds, potentially including the synthetic cannabinoids JWH-018 and JWH-073.[1–3] Although Spice is banned in some countries, it is legal to purchase JWH-018 and JWH-073. JWH-018 (1-pentyl-3-(1-naphthoyl)indole) and JWH-073 (1-butyl-3-(1-naphthoyl)indole) were designed by John W. Huffman to study cannabinoid receptor-ligand relationships. Initially used for research, JWH-018 and JWH-073 are now classified by the US DEA as a drugs of concern.[4,5] Because JWH compounds are synthetic chemicals, they are likely additives to Spice mixtures. Compared to THC, JWH-018 has greater affinity for central CB1 and peripheral CB2 receptors, and JWH-073 has greater affinity for CB1 receptors. Both compounds can be purchased from Internet vendors.[1,6] JWH-018 and JWH-073 are priced at $20/100 mg and are shipped as small plastic packets of off-white powder.[4] Analysis of this powder does not produce a positive result on the cannabinoid portion of the Microgenics Corporation qualitative drug of abuse immunoassay. *Conclusion:* JWH-018 and JWH-073 are designer drugs that do not react with the current drug of abuse screen. Many psychoactive substances do not react with qualitative immunoassays (i.e. buprenorphine, methadone and numerous benzodiazepines); synthetic cannabinoids should now be added to this list. Immunoassays' inability to detect synthetic cannabinoids may be of legal and medical importance. *References:* 1. Auwarter V, Dresen S, Weinmann W, et al. "Spice" and other herbal blends: harmless incense or cannabinoid designer drugs? J Mass Spectrom 2009; 44:832–7. 2. Microgram Bulletin, Volume 42, Number 9, September 2009, pages 73–76. Available at: http://www.justice.gov/dea/programs/forensicsci/microgram/mg0909/mg0909.pdf 3. Microgram Bulletin, Volume, 42, Number 3, March 2009. Available at: http://www.justice.gov/dea/programs/forensicsci/microgram/mg0309/mg0309.pdf 4. http://www.deadiversion. usdoj.gov/drugs_concern/spice/spice_jwh018.htm 5. http://www.deadiversion.usdoj.gov/drugs_concern/spice/spice_jwh073.htm 6. http://www.sacraresearch.com

Table 1. Clinical features on presentation to the ED

	Mean ± SD (range)
Heart Rate (bpm)	98.1 ± 26.6 (60 - 140)
Blood Pressure (mmHg)	140.8 ± 26.2 (100 - 192)
Temperature (°C)	35.8 ± 1.5 (33.6 - 38.1)
	Number (%)
GCS 15	6 (54.5%)
GCS ≤8	3 (27.3%)
Agitation	6 (54.5)
Seizures	3 (27.3%)
Vomiting	2 (18.2%)

292. JWH-018 & JWH-073 Synthetic Cannabinoids

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Objective: To describe the acquisition and laboratory analysis of JWH-018 and JWH-073, two cannabinoid receptor agonists synthesized by John W. Hoffman. Although they were initially used for research, their abuse has led the US DEA to classify them as drugs of concern.[1–4] *Methods:* We acquired JWH-018 and JWH-073 via the Internet. We ran both samples via the Microgenics Corporation qualitative drug of abuse immunoassay. In a second test, we spiked urine with these compounds and conducted a single step liquid extraction at pH 8–10 with ammonium hydroxide and dichloromethane. The extract was reconstituted with ethyl acetate. A sample was injected on Agilent 5973 GC/MS using chemstation software and an HP1 12 m capillary column. Chlorimipramine was the internal standard. *Results:* JWH-018 & JWH-073 were each priced at $20/100 mg and they were shipped as small plastic packets of off-white/brown colored powder. Analysis of this powder did not produce a positive result on the cannabinoid portion of the Microgenics Corporation

qualitative drug of abuse immunoassay at a 1000 ng/mL threshold. However, GC/MS analysis revealed an M + 1 peak at 328 (JWH-073) & 342 (JWH-018). *Conclusion:* Although JWH-018 and JWH-073 are undetectable by urine immunoassays, they both appeared as pure substances via GC/MS. As synthetic cannabinoids are increasingly available on the Internet as drugs of abuse, the ability to detect them will become increasingly important. *References:* 1. Auwarter V, Dresen S, Weinmann W, et al. "Spice" and other herbal blends: harmless incense or cannabinoid designer drugs? J Mass Spectrom 2009; 44:832–7. 2. Microgram Bulletin, Volume, 42, Number 3, March 2009. Available at: http://www.justice.gov/dea/programs/forensicsci/microgram/mg0309/mg0309.pdf 3. Microgram Bulletin, Volume 42, Number 9, September 2009, pages 73–76. Available at: http://www.justice.gov/dea/programs/forensicsci/microgram/mg0909/mg0909.pdf 4. http://www.deadiversion.usdoj.gov/drugs_concern/spice/spice_jwh073.htm

293. Cocaine and Pediatric Seizure

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Objective: To discuss cocaine-induced seizure in a 12-month old. *Case report:* A 12-month old male seized at home where crack cocaine was present. The infant experienced 3 prehospital generalized tonic-clonic seizures, requiring rectal and intravenous diazepam. After a fourth seizure and signs of adrenergic excess in the Emergency Department, he received lorazepam, phenytoin, phenobarbital, and rapid sequence intubation (with atropine, fentanyl, midazolam, and succinylcholine). Upon arrival, urine laboratory tests showed concentrations of cocaine (236 ng/mL) and benzoylecgonine (534 ng/mL). During a 4-day PICU stay, metabolic and traumatic cases of seizure were ruled out; the infant had an elevated serum troponin (0.83 ng/mL) and serum creatine phosphokinase (4570 U/L). The infant was discharged to the care of child protective services without further seizure activity. The infant's past medical history included *in-utero* exposure to HIV, but negative HIV serologies and normal CD4 counts. The patient was not breast-fed and had no family history of seizure. *Conclusion:* This infant suffered *status epilepticus* from acute cocaine toxicity. Cocaine induces catecholamine release and can cause seizure. The central nervous system in children may be especially sensitive to cocaine's effects because of incomplete development of the blood-brain barrier. Cocaine-seizures have been inferred by immunoassays for cocaine metabolites that may be detected in urine days after acute exposure in children.[1–4] Cocaine as a parent compound persists in serum and urine for 1–3 hours, allowing a temporal association between acute cocaine exposure and seizure to be made. Cocaine's presence in the urine confirms the association between seizure and cocaine exposure in this infant. Clinicians must consider acute cocaine intoxication as an etiology of pediatric seizure. *References:* 1. Olson K, Kearney T, Dyer J, et al. Seizures associated with poisoning and drug overdose. Am J Emerg Med 1994; 12:392–5. 2. Mott S, Packer R, Soldin S. Neurologic Manifestations of Cocaine Exposure in Childhood. Pediatrics 1994; 93:557–60. 3. Rivkin M, Gilmore H. Generalized Seizures in an Infant Due to Environmentally Acquired Cocaine. Pediatrics 1989; 84:1100–2. 4. Kramer L, Locke G, Ogunyemi A, et al. Neonatal Cocaine-Related Seizures. J Child Neurol 1990; 5:60–4.

294. Inhaled Albuterol as a Drug of Abuse

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Objective: Therapeutic drugs are taken in overdose in an attempt to "get high" by adolescents. These include methylphenidate, dextromethorphan, antihistamines, caffeine, and decongestants. We report a case of albuterol overdose taken by a 13 year old girl in an attempt to "get high." *Case report:* A 13 year old girl was told by a friend that she could get high by taking an overdose of her albuterol metered dose inhaler which delivered 120 micrograms of albuterol per inhalation. She reports taking 174 inhalations (20.88 mg) of albuterol over an eight minute period at school. Forty-five minutes later she reported to the school nurse with headache, nausea, blurred vision, feeling hot, and palpitations. She arrived in the Emergency Department two hours and 20 minutes after the overdose. Past medical history was attention deficit disorder, conduct disorder, and asthma. Social history was tobacco, alcohol, and illicit drug use. Medications were albuterol, birth control pills, and cough medicine containing dextromethorphan and guaifenesin. Vital signs on arrival at the Emergency Department were pulse of 116 per minute, respiratory rate of 20 per minute, blood pressure of 103/47 mm Hg. She was afebrile. A mild tremor of the hands was noted. Other than tachycardia and tremor, her physical examination was normal. Laboratory evaluation was remarkable for a potassium level of 2.6 meq/liter (normal range 3.5 to 5.0 meq/liter). Neutrophil count was elevated at 9.7 thousand/mL (normal range 1.8 to 7.7 thousand/mL). Other laboratory parameters were normal. Electrocardiogram showed a sinus tachycardia at 115/minute but was otherwise normal. Symptoms resolved gradually over two to three hours from the time of ingestion. Potassium rose to 3.3 meq/liter. She was discharged in the care of her parents after a period of observation. *Conclusion:* Albuterol can be added to the list of therapeutic medications that teenagers take in attempts to get high. Rather than a pleasurable experience, this girl became ill from her attempt with symptoms of headache, nausea, tremor, and palpitations. There was hypokalemia and neutrophilia as expected from an albuterol overdose.

295. Acute Myocardial Infarction Associated with Androgenic Anabolic Steroid Use

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Objective: Anabolic androgenic steroids (AAS) are synthetic derivatives of testosterone that enhance development of male characteristics (androgenic) and increase muscle mass (anabolic). Although AAS have legitimate use for uncommon endocrine disorders, they are often misused by athletes to gain a competitive advantage. Although the true incidence is unknown, some surveys estimate that over one million Americans may have used AAS. *Case report:* A 29-year-old man presented to the hospital complaining of intermittent left chest pain. He had no known past medical history and denied medication use other than intermittent paracetamol use for muscular pain. Traditional risk-factors for atherosclerotic heart disease were absent. In the ER, the left-sided chest pressure and shortness of breath recurred. On physical examination, the patient appeared uncomfortable and short of breath, but had normal vital signs. The ECG showed a sinus rhythm with T wave inversion in the inferior leads (II, III, aVF). Troponin I 2.27 ng/mL (<0.05 ng/mL). Urine toxicology screen was negative for cocaine, amphetamines and other common drugs of abuse. The patient was given 325 mg of aspirin and was transferred to a tertiary care hospital with a cardiology service. Approximately 1 hour after arrival, the troponin I was 20.71 ng/mL (<0.05 ng/mL). A non-ST elevation myocardial infarction was diagnosed and coronary angiography demonstrated a 99% mid right coronary artery occlusion. Two bare metal stents were placed and TIMI II flow was demonstrated after. He later admitted to taking fluoxymesterone for many years, with increased usage over the past year, but denied using any other supplementation such as clenbuterol or γ-hydroxybutyric acid as well as cocaine or amphetamine use. The patient was ultimately discharged in good condition on aspirin, atorvastatin, and clopidogrel. *Conclusion:* Adverse effects from AAS use include neuropsychiatry problems, hepatic involvement, as well as musculoskeletal complications such as tendon ruptures. Adverse cardiac events associated with AAS include hypertension, left ventricular hypertrophy, and myocardial infarction. AAS promote thrombogenesis, cause vasospasm, and accelerate atherosclerosis by altering lipid profile. This case supports a growing association between AAS use and acute MI.

296. Attempted Suicide, by Mail Order: *Abrus precatorius*

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Objective: Abrus precatorius is cultivated in many subtropical areas. The seeds exist in a variety of colors such as black, orange, and most commonly, glossy red. A black band is found at the end of the seed. The plant contains multiple pods which typically contain 3–5 abrus seeds. The seeds contain abrin, which inhibits ribosomal function halting protein synthesis leading to cellular death. *Case report:* A 20 year-old man presented to the ED complaining of vomiting and watery diarrhea for 6–8 hours prior to arrival. He denied any medication use, recent illness, travel, or changes in his diet. Initial vital signs were normal. The patient was diagnosed with viral gastroenteritis. During his evaluation, the patient admitted to feeling suicidal. While awaiting psychiatry evaluation the patient's father arrived with a box of small hard red seeds, which he believed that his son ingested in a suicide attempt. The seeds could not be identified by the staff. A picture of the seeds was transmitted by email to the New York City Poison Control Center, allowing their identification as *Abrus precatorius*. The patient was re-interviewed and admitted to chewing and swallowing 10 seeds. Given the potential toxicity of abrin, the patient was admitted to the intensive care unit. He continued to have frequent episodes of emesis as well as diarrhea. He gradually improved over two days. He admitted to ordering a box of *Abrus* seeds online from Asia after reading on the Internet about their use in suicide. He was eventually discharged for outpatient follow-up with no permanent sequelae. *Conclusion:* Abrin has an estimated human fatal dose of 0.1–1 μg/kg. Most cases of *Abrus* seed ingestions are unintentional and occur in children. Ingesting the intact seeds typically results in no clinical findings, as they pass through the gastrointestinal tract due to their hard shell. Abrin released during chewing is poorly absorbed systemically from the gastrointestinal tract. This causes the vomiting and diarrhea with resultant hypovolemia and electrolyte disturbances, which can be severe and life threatening, particularly in areas with less advanced healthcare systems. Management is primarily supportive.

297. Local Tissue Injury After Australian Snakebite

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Objective: To report an unusual (possibly unique) case of *Pseudechis australis* (*Elapidae*; mulga snake) envenoming causing significant local tissue necrosis and compare this to other cases of tissue injury after Australian snakebite. *Case report:* We here report a case of *Pseudechis australis* bite with significant local tissue injury, with uncertain contribution from first aid. The index case involved an 18 year old female bitten while asleep in bed in rural Australia in January by a *Pseudechis australis* (positive venom ID), treated promptly by PIB (pressure immobilisation bandaging) first aid, retrieved to a capital city and given appropriate antivenom (1 vial CSL Black Snake AV) <6 hours post-bite. She developed abdominal pain, myalgia, mild anticoagulant coagulopathy (peak aPTT 51sec), systemic myolysis (peak CK 50,350 U/L), anaemia (nadir HB 65

g/L) and mild thrombocytopenia (nadir $107x10^9$/L). Locally she developed an extensive area of full thickness skin necrosis at the bite site, on the upper thigh, requiring debridement and grafting. The contribution of first aid to the necrosis is uncertain and possibly minor, suggesting a primary venom effect. However, other cases of *P. australis* bites, with more severe systemic envenoming, have not shown local bite site necrosis, just swelling (JW experience over 33 years). One case with necrosis of the bitten thumb was associated with inappropriate extended (>2 hours) use of an effective digital tourniquet. Bites by other *Pseudechis spp*. and *Notechis spp*. resulting in skin injury or necrosis have mostly been similarly associated with local tourniquet application. *Conclusion:* We report a *P. australis* bite with significant systemic envenoming and necrosis of the bite site, without a clear contribution from first aid, distinct from previous experience where inappropriate first aid was clearly or highly likely to be a major cause of tissue injury. Doctors managing bites by *Pseudechis spp*. should be aware of the possibility of significant tissue injury, despite appropriate antivenom treatment. *References:* 1. White J. Local tissue destruction and Australian elapid envenomation. Toxicon 1986; S3:493–6. 2. White J. Overview of snake envenoming. In: Brent J, Wallace KL, Burkart KK, et al, eds. Critical Care Toxicology: Diagnosis and Management of the Critically Poisoned Patient. Philadelphia, USA: Elsevier-Mosby Inc, 2005:1051–74.

298. Collective Envenomation by *Physalia physalis* on the French Atlantic Coast

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Objective: Physalia physalis usually called Portuguese man-of-war is a jellyfish relative marine invertebrate present in the tropical seas. This species is rare in temperate seas.[1] The authors describe a case series of stings on the French Atlantic Coast after skin contact with these cnidarians. *Case series:* On August 25th, 2008, late in the afternoon on the beach of Biscarosse (Aquitaine region), 40 swimmers came out of the sea simultaneously for painful syndromes associated with skin lesions (local aspect of jellyfish stings). No animal was observed by the victims, who were managed immediately by the first-aid system on the beach. Decontamination with salt-water washing and tentacle removal was quickly performed for the 40 patients. Some of them needed pain-killers. Eight patients including one child (12 year old boy with intense pain and muscular cramps) were sent to the local hospital emergency unit because the clinical feature was severe: intense pain not improved by classical pain-killers, malaise, blood pressure disturbances, muscular cramps, respiratory distress syndrome (3 cases of respiratory distress treated with oxygen during 2 hours). All the patients recovered with symptomatic treatment allowing hospital discharge after 2 hours of medical care. In order to discover which marine invertebrate was at the origin of such an epidemic poisoning, the coastguards studied the sea water around the area of the collective envenomation: they captured 2 specimens of marine animals with long tentacles, identified by biologists of the French Institute for Marine Life (IFREMER) as *Physalia physalis*. The follow-up during 10 months of the 8 victims with clinical features of severe envenomation emphasized the long-term course of the local signs: local pain during 4 weeks, painful scars, recurrent inflammation of the involved skin surface. *Conclusion:* As the Portuguese man-of-war is rare and sporadic in the North Atlantic Ocean, this case series of 40 envenomations induced by 2 large specimens is the first one observed in such a northern geographical localisation. *Reference:* 1. Bedry R, Pillet O, Rivet P, et al. Epidemiologie des aggressions par animaux venimeux marins sur le littoral atlantique sud pendant la période estivale 1996. Réan Urg 1996; 7:375–80.

299. Follow-up on Mushroom Exposures and Poisonings in the Danish Poison Information Centre

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Objective: Management of mushroom poisonings is complicated due to inclusion of different toxicological effects, difficulties with identification and evidence mainly based on case information from the most severe poisonings.[1–3] The majority of mushrooms are associated with little risk, thus to attain a rational approach to the poisonings we have evaluated all mushroom exposures handled by the Danish Poison Information Centre (DPIC) during one year. *Methods:* At all mushroom related contacts to the PIC a structured interview was performed, the mushroom was photo-identified and, if possible, physically identified by an expert. Follow-up interviews were performed after 2–7 days and hospital discharge records were requested. *Results:* In total, 160 calls on mushroom exposure were received (1% of calls). Digital photos identified 132 (83%) of the mushrooms; two of these were *Amanita phalloides* one *Gyromitra esculanta*, and 25 were other toxic or possibly toxic mushrooms. Edible mushrooms were identified in 33 cases. Children below the age of 6 years were involved in the majority of calls (85%). Most of these children (95%) remained asymptomatic and none were admitted to hospital although some had tasted potentially toxic mushrooms. The only severe poisoning were the two cases where *Amanita phalloides* had been eaten for a meal. *Conclusion:* The vast majority of calls on mushrooms to the Danish PIC were infants and toddlers accidentally eating part of a non-toxic mushroom or a non-toxic amount of a possibly toxic mushroom. Identification by digital photography is a feasible and cost effective mean for mushroom identification. *References:* 1. Escudie L, Francoz C, Vinel J-P, et al. *Amanita phalloides* poisoning: Reassessment of prognostic factors and indications for emergency liver transplantation. J Hepatol 2007; 46:466–73. 2. Bedry R; Baudrimont I, Deffieux G, et al. Wild-mushroom intoxication as a cause of rhabdomyolyses. N Engl Med 2001; 345:798–802. 3. Meunier BC, Camus CM, Houssin DP, et al. Liver transplantation after severe poisoning due to amatoxin-containing Lepiota - Report of three cases. Clin Toxicol 1995; 33:165–71.

300. Human Envenomation by *Bitis parviocula* (Ethiopian Mountain Adder)

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Objective: The Ethiopian mountain adder (*Bitis parviocula*) is a venomous viper species found only in the highlands of south-west Ethiopia and expensively sold on the black market of snake keepers in Europe and the USA. While zoological information of this extremely rare specimen is available, analyses of venom composition are missing. The first case of a bite by this species has been recently reported in the USA.[1] To our knowledge no other human cases are published so far. We report the second case of human envenomation by *Bitis parviocula*. *Case report:* A 44 year-old man was bitten on the third finger of his left hand while attempting to feed his specimen of *Bitis parviocula* (identified by a herpetologist). He presented to the emergency department one hour after the accident with local pain and mild swelling which peaked on the 3rd day. Clinical symptoms were absent apart from the local involvement. Laboratory findings were found to be within normal limits with the exception of: D-Dimer, peak 939 mcg/L within first 24 hrs (n.v. <250); platelets $83,000/mm^3$ (n.v. 140,000–440,000). The ECG showed no abnormalities. Two vials of SAIMR Polyvalent Snake Antivenom were given 18 hours following the accident and three more were administered 7 hours later for worsening local oedema. Due to the onset of progressive circulatory impairment at left-hand level (patchy hypoaesthesic areas, cool bitten finger, bullous lesions around the bite), a fasciotomy was performed on 5th day. Ten sessions of hyperbaric therapy were administered. The whole left forearm returned to its normal volume within two weeks, whereas the bitten finger presented a persistent claw-like pattern as a complication of the fasciotomy. *Conclusion:* The first case of human envenomation by *Bitis parviocula* described in the literature was registered in Texas in May 2009. Our case occurred two months later in Italy, being the first event in Europe. Clinical symptoms consisted of local reactions with pain and swelling. Systemic toxicity was absent. As there is no specific antivenom available for this species, SAIMR Polyvalent Antivenom was administered for local swelling. This measure was ineffective in preventing the development of a compartment syndrome. *References:* 1. Fernández MC, González A. Ethiopian Mountain Viper Envenomation in South Texas. Clin Toxicol 2009; 47:712.

301. Yew can be Really Poisonous to You

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Objective: To show that ingestion of *Taxus* can result in significant morbidity. *Methods:* In a retrospective study all cases with the ingestion of yew were analyzed. The study comprised two poisons centres over a ten months period. Notification of the severity according to PSS. *Results:* The time period was from January until October 2009. Poisons centre A: 215 exposures with *Taxus*; 57 of them with leaves, twigs or preparations of tea. Three patients developed severe symptoms (5%). Poisons centre B: 113 cases; 6 patients with severe symptoms (5%). To illustrate symptoms and treatment of severe yew poisoning two cases are presented. Patient 1: A 16-year-old girl was found unconscious with no measurable blood pressure. No history of severe neurological or cardiac diseases. Immediate start of cardiopulmonary resuscitation (duration: 2 hours 45 minutes). Administration of epinephrine, extracorporeal membrane oxygenation, pacemaker and therapeutic hypothermia to 33 °C was started. Interrogation of the parents resulted in the discovery of *Taxus* leaves and tea under the bed of the girl. Decontamination by gastroscopy 6 hours after the ingestion with the removal of many *Taxus* leaves. One week after this suicidal ingestion the patient was stable and psychiatric treatment could be initiated. Patient 2: A 59-year-old woman deliberately drank tea from *Taxus* leaves with alcohol. She was found unconscious and bradycardic after a bicycle accident. Decontamination was started 2 hours after the ingestion by gastroscopy and many *Taxus* leaves were removed; activated charcoal was administered thereafter. Due to cardiac arrest cardiopulmonary resuscitation was started. Persisting severe dysrhythmias were treated by defibrillation, pacemaker and lidocaine. Finally a successful stabilization of the cardiac rhythm was achieved and the patient could be discharged to the psychiatric department. *Conclusion:* The ingestion of *Taxus* leaves or the extract of yew plants can result in life threatening symptoms. Decontamination with gastroscopy and administration of activated charcoal can be useful after several hours. Resuscitation should be practiced for longer than usual. *Reference:* 1. Krenzelok E, Jacobsen TD, Aronis J. Is the Yew Really poisonous to You? Clin Toxicol 1998; 36:219–23.

302. A Heavy Fish

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Objective: To find a bio-umoral marker that could help physicians to formulate a correct diagnosis in Histamine Fish Poisoning (HFP) and consequently to

choose the best therapeutic strategy. HFP is a complex of symptoms caused by biogenic amines, mainly histamine, contained in seafood. The diagnosis is quite difficult as the symptoms of this particular condition are similar the symptoms of a normal allergic reaction. *Methods:* We collected 10 cases (3 male and 7 female) of HFP and 50 non-HFP patients (35 female and 15 male). On examination seven of them had a diffuse erythematous rash over the face, arms, legs and torso, flushing, diarrhoea, vomiting, tachycardia, itching and hypotension. Four patients presented with dizziness, nausea and abdominal pain. Laboratory examinations were carried out, including kidney and liver function, clotting system study and tryptase serum levels in samples obtained before any therapeutic intervention, by fluoroenzymeimmunoassay method (Phadia ImmunoCAP™). *Results:* As expected, tryptase serum levels of most of the 50 patients with allergic or anaphylactic disorders were highly increased above normal value, whilst all the tryptase serum levels of the 10 patients with HFP were within the normal range. *Conclusion:* An early diagnosis and treatment is the correct pathway to an effective therapy: a level of serum tryptase within the normal range in patients with clinical signs of histamine mediated reaction and anamnesis compatible with HFP is a useful indicator to support the diagnosis.

303. Tiger Snake (*Notechis scutatus*) Bite with Late Developing Myolysis and Thrombotic Stroke

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Objective: To report a very unusual case of tiger snake (*Elapidae*; *Notechis scutatus*) bite with aberrant venom detection results, delayed myotoxicity and thrombotic stroke. *Case report:* A 63 year old female was bitten above the ankle by a witnessed snake, which was killed and later identified as an adult tiger snake. A PIB (pressure immobilisation bandage) was applied as first aid and she presented at hospital 1 hour post-bite. Bite site venom detection was positive for death adder. She complained of severe local pain, with local bruising and swelling, but no systemic signs of envenoming and normal coagulation, CK, so no antivenom given. She had a recent history of cough and basal crackles on examination. Only LFTs were initially abnormal, and these improved over several days. Coagulation remained normal, except elevated d-dimer on day 2. CK rose from day 3, peaking on day 10 (17852 U/l). Chlamydia serology positive (day 2 & 10) but antibody titre negative. CXR showed bibasal collapse. On day 5 the patient developed headache, vomiting and on day 10 worsening, when CT head showed a R parietal lobe lesion consistent with venous thrombosis. The cause was not apparent, and late envenoming was considered unlikely, so antivenom was not given. She improved and underwent rehabilitation and at 3 months has no residual symptoms or signs. There are no previously reported cases of thrombotic stroke following Australian snakebite, but it is unclear if envenoming was causative in this case, given the late onset. *Conclusion:* Despite evidence of only mild systemic envenoming, consistent with a tiger snake, but with erroneous venom detection, this patient developed a severe adverse event, linkage to envenoming being uncertain. However, thrombotic strokes are now being described in isolated cases for other snake species, indicating this may be a rare complication for snakebite, not just restricted to the two known thrombotic species from the Caribbean, *Bothrops lanceolatus* and *B. caribbaeus.*

304. Cholinergic Symptoms Due to Brown Fly Agaric Poisoning

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Objective: The Finnish Poisons Information Service (FPIC) annually receives about a dozen inquiries concerning brown fly agaric mushroom, *Amanita regalis*. In most cases it has been confused with the edible parasol mushroom, *Macrolepiota procera*. Brown fly agaric is often considered just as a brown variation of fly agaric, *Amanita muscaria*. Also according to current sources of information it contains muscimol and ibotenic acid. However, in a few poisonings reported in Finland and in Germany, the symptoms were not characteristic of the mushrooms containing ibotenic acid and muscimol. In those cases symptoms began usually 1–2 hours after ingestion and the patients had gastrointestinal symptoms, unconsciousness, convulsions and cholinergic symptoms.[1,2] We now report a new case of poisoning due to brown fly agaric demonstrating cholinergic symptoms. *Case report:* In August 2009 a 62-year-old man ate several brown fly agarics believing he had eaten parasol mushrooms. Soon after ingestion he developed gastrointestinal symptoms and confusion. Four hours after ingestion and admission to the hospital the patient was sweating profusely, had muscle jerks and agitation. Activated charcoal, atropine and diazepam were given. About 6 hours later the patient was unconscious, but responded to painful stimuli with trembling and twitching. Nine hours after ingestion, the patient had apneic periods and the muscle twitching continued. Flumazenil was given, because he had received slightly excessive doses of diazepam. Flumazenil relieved both muscle tension and breathing. Symptoms gradually resolved and the patient was discharged 22 hours after the ingestion of the mushrooms. *Conclusion:* Our case provides further support that brown fly agaric mushroom ingestion causes cholinergic symptoms different from the typical ones seen after ingestion of mushrooms containing muscimol and ibotenic acid. *References:* 1. Elonen E, Tarssanen L, Härkönen M. Poisoning with Brown Fly Agaric, Amanita Regalis. Acta Med Scand 1979; 205:121–3. 2. Hentschel H, Volkmann H, Grummt B, et al. Poisoning with Amanita regalis (Brown Fly Agaric). Clin Toxicol 2004; 42:512.

305. Multiple Splenic Infarctions After Viper Envenomation

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Objective: To describe a case of viper envenomation where a progressive increase of D-dimer levels was correlated to multiple splenic infarctions. *Case report:* A 66-year-old man was admitted to the ED ten hours after a viper-bite on his right hand: a painful oedema was present up to the elbow and the patient suffered several episodes of diarrhoea. The next day the oedema appeared unchanged while laboratory tests revealed an increase of D-dimer (3,916 ng/mL), WBC (20,700/mm^3), AST (106 IU/L) and CPK (1247 IU/L), so treatment with low weight heparin (LWH) was started; the patient remained clinically stable and an echo-colour-Doppler was negative for signs of thrombosis. The following day D-dimer was 20,000 ng/mL and started decreasing during the following 24 hours with levels that ranged between 10,000 and 14,000 ng/mL until discharge. From day 4 the oedema progressively improved; in the meanwhile LWH was suspended because the patient developed a mild haemolytic anaemia (haemoglobin 11.8g/dL). On day 8 WBC and platelets decreased to 14,000 and 76,000/mm^3 respectively; D-dimer was 13,000 ng/mL. On day 9, an abdominal echography showed a spleen enlargement (up to 16 cm) with non-homogeneous areas. A contrast CT-scan was immediately performed, that revealed areas of hypodensity due to multiple infarcts occupying most of the parenchyma; no signs of thrombosis were detected. Considering the stable levels of haemoglobin and platelets, LWH was re-started at low dosage. The areas of infarction slightly reduced during the following 5 days, so the patient did not undergo splenectomy and was discharged on day 21 with a program of follow-up abdominal echographies. At 6 months from the viper-bite parameters had normalized and non-homogeneous areas were still present in 50% of the spleen parenchyma; D-dimer was 14,000 ng/mL. *Conclusions:* Considering the limited severity and the stability of clinical conditions during the first 24 hours, Fab-fragments were not administered. The progressive increase of D-dimer suggested looking for possible thrombosis despite improvement of general condition. In this case D-dimer has been an important marker for identification of severe systemic effects of viper venom and permitted identification of rare complications such as splenic infarction.

306. Familial Tetrodotoxin Poisoning in French Guiana

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Introduction: Tetrodotoxin poisoning is a rare event outside Japan where this marine poisoning is well known. The authors describe a case of collective poisoning in French Guiana where porcupinefish and pufferfish are usually not considered to be edible. *Case series:* Two adults and a 2-year-old child had a meal composed of 3 unidentified fresh fish given by a fisherman. They removed the skin and internal organs, washed, grilled and then ate the flesh. The first adult (case 1) ate one fish, the other adult ate half a fish, and the child ate only a spoonful. Case 1: A 54-year-old man was admitted to an emergency unit at H10 with slurred speech and paresis of the lower limbs. Cardiorespiratory arrest occurred suddenly several minutes later, causing anoxic complications. This patient died on D47 (D2 serum tetrodotoxin concentration: 18.5 ng/mL). Case 2: A 34-year-old man presented at H16 with oral dysaesthesia and dizziness which had appeared several minutes after the meal. Muscle weakness, ataxia and slurred speech were also reported. At H35, the clinical features included dilated pupils, hypersalivation, diminished reflexes and sinus bradycardia (55 bpm) and respiratory depression requiring mechanical ventilation. All symptoms progressively resolved after H60 and extubation was possible on D4. Case 3: The child was admitted at H16 with ataxia. Hypersalivation, diarrhoea, muscle weakness, paraesthesia and a vestibular syndrome were observed. Progressive recovery was reported from D3 and was complete on D4. *Discussion:* Tetrodotoxin poisoning was proposed on the basis of the clinical history and clinical features of the 3 patients and was confirmed by blood assay in case 1. Several fish species in French Guiana can cause tetrodotoxin poisoning; tetrodotoxin is mainly found in the liver, ovaries, intestine, and skin of the fish. In the cases reported here, all these parts had been removed before cooking. However, tetrodotoxin is also present in lower concentrations in the flesh and the large amounts ingested by the 2 adults probably account for their severe poisoning. The interval between the meal and onset of respiratory paresis/paralysis was unusually prolonged. Such a delayed onset has been previously reported in only 2 cases.

307. A Bittersweet Symphony

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Objective: To describe an unusual cyanide poisoning due to ingestion of large quantities of seeds containing amygdalin which caused typical symptoms linked to inhibition of cellular respiration. *Case report:* A young woman of 35 years, mentally disturbed, was admitted to our ED. The parents said they had found her in the living room, surrounded by apricots from which she had extracted the core, eating the kernels. According to anamnesis, it seems that the woman had swallowed 40 to 60 kernels 30 minutes before arrival at ED.

The woman, not cooperating, was asymptomatic, TA 120/70, FC 120, FR 20, T 37.5 °C, O_2 sat 98%. A slight metabolic acidosis was detected at arterial blood gas analysis. She was subjected to gastric lavage, 70 grams of activated charcoal and 30 grams of magnesium sulphate were administered with hydration and ECG monitoring. Ninety minutes after ingestion, the patient experienced headache, nausea and dyspnea. Vital parameter changes: TA 75/50, FC 145, FR 28, sat O_2 94%; acidemia was present. Two vials of amyl nitrite were administered via inhalation with 50 mL sodium thiosulfate 25% I.V. (infusion rate: 5 mL/min). After this therapy, a methemoglobinemia of 10% was measured. The vital signs slightly improved, allowing the intravenous administration of 5 g of hydroxocobalamin I.V. in 30 minutes, with clinical improvement in a short time. During treatment no significant ECG changes were noted. The patient underwent clinical observation, maintaining levels of methemoglobinemia around 10% through the inhalation of ampoules of amyl nitrite for 4 hours after hydroxocobalamin administration. After a 24 hour stay in the Clinical Toxicology Unit, the woman was transferred to the psychiatry department for further observation and treatment. *Conclusion:* Apricot kernels have usually a pleasantly bitter aftertaste and they are used in confectionery as flavouring, as an ingredient in macaroons, in syrups or liqueurs and generally in conjunction with sweet almond to spice up the taste. However, their consumption is limited to use as an aromatic as apricot leaves and flowers contain a cyanide derivative, amygdalin, which, at high doses, would be highly toxic.

308. Coagulopathy Following Copperhead Snakebites

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Objective: Optimal management of copperhead, *Agkistrodon contortrix*, snakebites and their risk for coagulopathy is not clear.[1,2] Serial coagulation studies are commonly performed, often in the setting of hospitalization. We determined the incidence of coagulopathy in copperhead snakebites. *Methods:* We performed a retrospective review of all venomous pediatric snakebites presenting to St. Louis Children's Hospital over 15 years and of all venomous snakebites in adults presenting to Barnes-Jewish Hospital over 7 years. Nonvenomous snakebites and bites from other animals were excluded. Charts were reviewed noting patient demographics, certainty of snake identification - positive, presumptive, or unknown, bite location on patient, laboratory coagulation values, and clinical bleeding complications. *Results:* We yielded 471 records of which 339 were excluded based on the above criteria. Of the 132 remaining charts, we excluded 25, including 3 re-admissions, 1 dry bite, 1 miscoded chart, 1 admission after admission elsewhere, 5 inaccessible charts, 8 rattlesnake bites, 1 cottonmouth bite, 4 non-native snakebites, and 1 unconfirmed snakebite. The final data set included 107 venomous snakebites, of which 18 were positively identified as copperheads, 52 presumptively identified, and 37 unknown. In no case did bleeding complications develop. Mean and median values for the most abnormal coagulation values for each patient by degree of certainty were: positively identified copperheads- PT 12.9/13, PTT 30.6/30.3, INR 1.08/1.06, Plt's 265/259, fibrinogen 226/229; presumptively identified copperheads - PT 14.0/14.2, PTT 29.4/29.2, INR 1.13/1.12, Plt's 244/230, fibrinogen 269/261, and unknown - PT 14.2/14.3, PTT 29.8/29.7, INR 1.12/1.11, Plt's 269/249, fibrinogen 286/272. *Conclusion:* In snakebites identified as copperheads, it is safe to forego hospital admission for the purpose of serial coagulation testing in both adult and pediatric patients thereby saving significant money and patient discomfort. *References:* 1. Garrison J, Caldera J, Velez L, et al. Lack of Coagulopathy from American Copperhead Envenomation, Regional Poison Center Experience. Clin Toxicol 2005; 43:477. 2. Thorson A, Lavonas E, Rouse A, et al. Copperhead Envenomations in the Carolinas. Clin Toxicol 2003; 41:29–35.

309. *Cortinarius orenalloides* Poisoning: Three Years Follow-up of Five Members of a French Family

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Case report: An 11-year-old boy and his 48-year-old father presented with a 3-day history of abdominal pain, vomiting, marked asthenia, deep thirst and oliguria. The young boy's blood samples showed pH 7.38, creatinine 1137 micromol/L, K 9.1 mmol/L, Na 123 mmol/L, chlorine 92 mmol/L; his ECG was typical of severe hyperkalaemia. Forty-eight hours continuous hemodiafiltration was then required. Father's serum creatinine was 840 mmol/L with K 4.6 mmol/L. This orellanus syndrome began two days after ingestion (twice) of a meal containing wild mushrooms. Acute renal failure (ARF) was documented and required dialysis in the two cases. Three other members of the family who had ingested a smaller amount showed no or few symptoms but were found to have ARF which was marked in one case despite normal physical examination. Renal biopsy, performed in the three patients who had severe ARF, documented acute tubular necrosis with tubulitis (polymorphonuclear cells extended into the walls and lumina of tubules). The diagnosis was confirmed 3 weeks later since fungal spores of *Cortinarius orellanoides* were observed in the contaminated meal by light microscopy. Additional renal biopsies (3) were performed in the young boy and showed severe interstitial fibrosis: long term renal replacement therapy was necessary until he benefited from successful renal transplantation. Partial or complete recovery was obtained in the four other patients. *Discussion:* ARF following ingestion of *Cortinarius orellanoides* is due to the fungal toxin orellanine. Intoxication by *Cortinarius speciosissimus* is characterized by acute tubular necrosis associated to tubulitis with neutrophils. It is rare and occurs in Europe and North America every year with edible mushrooms. The detection of orellanine in biological fluids cannot be obtained in clinical practice. Orellanine nephrotoxicity is mediated by oxidative stress, including a virtual shutdown of important antioxidative enzymes, leading to be careful for antioxidant treatment as HC-SOD. *Conclusion:* Familial examination is mandatory in mushroom poisoning if *Cortinarius* species is suspected. *References:* 1. Nilsson UA, Nyström J, Buvall L, et al. The fungal nephrotoxin orellanine simultaneously increases oxidative stress and down-regulates cellular defenses. Free Radic Biol Med 2008; 44:1562–9. 2. Saviuc P, Flesch F, Danel V. Intoxications par les champignons: syndrome majeurs. Encycl Méd Chir (Elsevier SAS, Paris, tous droits réservés), Toxicologie-Pathologie professionnelle, 16–077-A-10, 2003:10.

310. Butterfish - Delicious Food or Revenge of a Delicacy?

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Objective: In 2003, BfR had for the first time warned against the consumption of "butterfish" (escolar) on its homepage because of case reports from Australia although no cases had become officially known in Germany up to that time. After the press release, health complaints caused by "butterfish" were reported by more and more persons so that differentiated accounts of cases could be published as part of the regular annual reporting of the BfR Centre for Documentation and Assessment of Poisonings. Recently, the number of inquiries about "butterfish" from the general public has increased to such a degree that BfR will deal with the topic in more detail in the context of early risk identification. *Methods:* All inquiries on "butterfish" received since the beginning of compulsory notification in 1990 were retrospectively evaluated and recorded in the form of case reports. *Results:* Since 2004, BfR has registered 39 cases of health disorders after consumption of "butterfish". In 38 cases, health disorders were rated as minor, and in one case, as moderate due to an underlying disease. Typical manifestations included nausea, colicky abdominal pain and diarrhoea with characteristic orange oily stools and headache. Four persons required inpatient treatment. Based on the uniform symptomatic picture of the 38 cases evaluated, the causal relationship has been rated as "probable". *Conclusion:* In predisposed persons, consumption of "butterfish" or "butter mackerel" of the species, *Lepidocybium flavobrunneum* and *Ruvettus pretiosus* may result in mild gastrointestinal symptoms with orange oily stools and headache, irrespective of the quantity consumed. Therapy will depend on the symptoms and/or consist of a special diet. Symptoms are presumably caused by the presence of not readily or not digestible wax esters accounting for 90% of the oil of these fish species. Since manifestations included headache, it has been assumed that other factors such as certain fish proteins having allergenic activity, or biogenic amines are also involved which may form during extended storage. Possibly, health impairments can be avoided by suitable preparation practices such as discarding the oil leaking from the food. BfR will look into health complaints caused by "butterfish" in more detail.

311. Fish Consumption and Rhabdomyolysis: A Review

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Objective: To review the literature on the association between fish ingestion and rhabdomyolysis, in order to analyze a possible outbreak of rhabdomyolysis after eating fish (described in the literature as Haff disease), in Amazonas, Brazil. *Methods:* We searched electronic databases (Medline, Lilacs and Scielo) and abstracts available from American, European and Brazilian associations of clinical toxicology; in addition, all references in the articles reviewed were searched. All studies about rhabdomyolysis and fish ingestion published in English, Spanish or Portuguese were selected. *Results:* We assessed five articles[1–5] that recorded 19 cases. The fish eaten had been cooked in all but one of the cases. Both freshwater and saltwater fish were implicated. The incubation time ranged from 4 to 12 hours. Palytoxin was the possible causative agent in two cases; in others, the toxin was not identified. All of the patients presented elevated creatine kinase (the marker for rhabdomyolysis). Other common symptoms were vomiting (10), nausea (9), shortness of breath (8), sweating (7), myalgia (6), muscle stiffness (5) and myoglobinuria (4). One patient died after acute renal failure and cerebral death. Intravenous hydration was the treatment of choice in most cases. Patients that survived the event recovered from all their symptoms, although in some cases, the clinical effects remained for some weeks or months. *Conclusion:* The occurrence of rhabdomyolysis after eating fish, or Haff disease, usually leads to favorable outcomes. The treatment is supportive and consists of administering large volumes of fluid to prevent myoglobin toxicity in the renal tubules. *References:* 1. Shinzato T, Furusu A, Nishino T, et al. Cowfish (Umisuzume, Lactoria diaphana) poisoning with rhabdomyolysis. Intern Med 2008; 47:853–6. 2. Langley RL, Bobbitt WH III. Haff disease after eating salmon. South Med J 2007; 100:1147–50. 3. CDC. Haff disease associated with eating buffalo fish-United States, 1997. MMWR 1998; 47:1091–3. 4. Okano H, Masuoka H, Kamei S, et al. Rhabdomyolysis and myocardial damage induced by palytoxin, a toxin of blue humphead parrotfish. Intern Med 1998; 37:330–3. 5. Krishna N, Wood J. It looked like a myocardial infarction after eating crawfish. . . ever heard of Haff disease? Louisiana Morbidity Report 2001;12.

312. Human Accidents Involving *Rhinocricus spp*, a Common Millipede Found in Urban Areas of Brazil

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Objective: To describe and discuss a series of clinical cases of dermal accidents with *Rhinocricus spp* secretions. *Case series:* We describe 4 cases of skin involvement after accidental contact with the secretions of *Rhinocricus spp*. The most important millipede species causing accidents in Brazil is *Rhinocricus padbergi* (order *Spirobolida*, family *Rhinocricidae*), a vegetarian scavenger distributed from Central to South America. Case 1: A 12-year-old-boy putting on a sock had not realized that a *Rhinocricus spp* was inside it. He felt a slight pain in the toe and in the medial face of the foot. Soon after he observed a dark reddish spot forming locally. No medication was prescribed and twelve days later the lesion had completely vanished. Case 2: An 8-year-old-boy accidentally smashed a *Rhinocricus spp* with his left toe while putting on a shoe. He immediately felt a burning sensation and his skin became tanned with a reddish halo around the lesion. We lost the child to follow up soon after. Case 3: A 2-and-half-year-old-boy noticed something bothering his foot inside the shoe. Taking it out, his mother observed several dark reddish spots on the sole of the foot and an animal identified as a *Rhinocricus spp*. No pain was referred and the lesions lasted some weeks until they resolved without any medication. Case 4: A 46-year-old-man observed an animal described as a millipede (*Rhinocricus spp*) inside his socks 4 hours after putting on his shoes. His second toe was completely black spotted resembling a necrotic lesion. He felt no pain. *Conclusion:* Despite the frightening necrotic appearance of *Rhinocricus spp* skin lesions, only very mild inflammation and no necrosis are present. Analysis of the content of 50 glands of these animals captured in the south-east region of Brazil identified 2-methyl-1,4-benzoquinone and 3,3a,4,5-tetrahydro-1H-pyrrolo-[2,3-b] pyridine-2,6-dione as the substances responsible for the lesions. Benzoquinones are strongly irritant and persistent compounds, working very well as insect repellents, being toxic to a great variety of other parasites and pathogens. They have tanning properties. No systemic toxic effects have been described so far after skin contact with benzoquinones.

313. Two Related Cases of Erucism in Philadelphia, Pennsylvania, USA

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Objective: Only about 12 families of caterpillars worldwide can cause significant problems to humans. However, recognition and proper management of caterpillar envenomations is important. *Case report:* Two homeless men sleeping underneath a sycamore tree in a local park presented to a local emergency department one day apart with similar clinical presentations. Two caterpillars fell from the tree onto the first patient's left ear and the left side of his neck; he brushed them off with his hand, which then came into contact with his right shoulder. He experienced immediate pain with subsequent local edema, pruritus, and a maculopapular rash with wheal formation involving the ear, neck, and shoulder. The second patient woke up in the middle of the night to find two hairy green caterpillars, each with a central orange spot, crawling on the right side of his neck and on his left upper arm and forearm. He developed an eruption similar to that of the first patient. Both patients responded well to diphenhydramine 25 mg intravenously in the emergency department and were discharged. Repeated searches of the park failed to reveal caterpillars, but one of the patients positively identified a photograph of the saddleback, or packsaddle, caterpillar (*Acharia stimulea*) as the type of caterpillar that had fallen onto him. *Conclusion:* Depending upon the species, envenoming, or stinging, caterpillars can cause erucism (caterpillar dermatitis), lepidopterism (with systemic manifestations), dendrolimiasis (with osteoarthritis), ophthalmia nodosa (from corneal penetration and intraocular migration of setae), and (in the case of South American *Lonomia* caterpillars) consumptive coagulopathy with secondary fibrinolysis, intracerebral hemorrhage, acute renal failure, and death. It is important to realize that although most brightly colored caterpillars are harmless to humans, exposure to seemingly innocuous caterpillars can lead to significant clinical effects. *References:* 1. Diaz JH. The evolving global epidemiology, syndromic classification, management, and prevention of caterpillar envenoming. Am J Trop Med Hyg 2005; 72:347–57. 2. Malaque CMS, Andrade L, Madalosso G, et al. Short report: A case of hemolysis resulting from contact with a Lonomia caterpillar in southern Brazil. Am J Trop Med Hyg 2006; 74:807–9.

314. Poisoning by *Amanita Phalloides*

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Objective: To describe the clinical findings, treatment and outcome of an accidental ingestion of *Amanita phalloides* mushroom by a family of five. *Case report:* A family enjoyed a meal made of *Amanita phalloides*. The mushrooms were mistaken for other edible species. Symptoms (nausea, vomiting, diarrhoea, chills) began 11–12 hours later. They were admitted to a local area hospital where all initial laboratory results were unremarkable. At first *Amanita phalloides* poisoning was not suspected and the patients received only intravenous hydration. By approximately 40 hours post ingestion all had developed laboratory evidence of toxic hepatitis and they were transferred to Tartu University Hospital into the intensive care unit. Silibinin is not available in Estonia and thus all patients were treated with multiple dose activated charcoal, plasmapheresis, hyperbaric oxygen therapy (HBO) and high-dose intravenous penicillin. Activated charcoal adsorbs the amanitins and penicillin acts possibly hepatoprotectively. It is considered that plasmapheresis may be effective shortly after ingestion, but because of the absence of prospective controlled studies the method is not recommended as a standard therapy. The mechanism of action and efficacy of HBO in toxicology continue to be investigated. An 89 year old woman (co-morbidities: diabetes, hypertonia) developed profound hepatotoxicity (ALT 3722, AST 7119) and renal failure (creatinine 818, urea 38.8). Renal failure improved after 4 procedures of haemodialysis. The patient was discharged after 20 days with an ALT of 26, AST of 21, creatinine of 306 and urea of 22.8. The four other patients developed moderate hepatotoxicity with following laboratory results - 33 year old woman ALT 3862, AST 4628; 13 year old boy ALT 2184, AST 2823, two 14 year old boys ALT 3019/1744, AST 3062/1346. They were discharged after 10 days with moderately elevated hepatic markers (33 year old woman ALAT 109, ASAT 28; 13 year old boy ALT 101, AST 51; two 14 year old boys ALT 114/96 AST 45/35). *Conclusion:* When intravenous silibinin is not available a combination therapy of high-dose intravenous penicillin, plasmapheresis and multiple dose activated charcoal is effective in the treatment of *Amanita phalloides* poisoning. The role of HBO remains questionable.

315. First Confirmed Case Report of Cutaneous Loxoscelism Caused by *Loxosceles anomala*

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Objective: To report the outcome of a patient bitten by *Loxosceles anomala*. *Case report:* A previously healthy 35-year-old female was bitten on the anterior right thigh by a brown spider while she was dressing in her trousers (1 p.m., T0); the spider was killed and stored for identification. Clinical evolution at post-bite times (T, in h) was: T0 - relatively painless bite with mild itching. T24 - progressive local swelling, with induration; transient generalized erythrodermic rash, more intense on the face and trunk. T48 - progressive local discomfort with pain of increasing intensity (stinging burning sensation) and changes in the lesion pattern. T57 - photos of the lesion sent by e-mail to the main author revealed an irregular blue plaque surrounded by an erythematous halo. There was no fever, pallor, jaundice or change in urine color; a presumptive diagnosis of cutaneous loxoscelism was considered. T60 (admission to the university hospital) - physical examination revealed an irregular lesion (6x4 cm) with the characteristics described above, located over an area (20x12 cm) of indurated swelling. Five vials of anti-arachnidic antivenom [AV, Instituto Butantan, Brazil; F(ab´)2 antibodies against *Loxosceles gaucho*, *Phoneutria nigriventer* and *Tityus serrulatus* venoms] were infused without adverse effects. T68 - reduction in the pain and cessation of lesion progression; the patient was discharged. Day 5 - the patient brought the spider that had caused the bite, subsequently identified as an adult male *L. anomala*. There was no dermonecrosis or hemolysis and complete lesion healing was observed by day 55. *Conclusion:* Brown spider bites are common in Brazil and are caused mainly by *L. intermedia, L. laeta* and *L. gaucho*; no confirmed bites by *L. anomala* have previously been reported. The clinical features and outcome described here were compatible with cutaneous loxoscelism and similar to those reported for other *Loxosceles* species. Antivenom has been used to treat clinical loxoscelism in Brazil since the 1960s and shows good cross-reactivity in neutralizing the dermonecrotic and lethal activities of several *Loxosceles* venoms in rabbits. The inhibition of lesion progression observed following AV administration suggested that in this case AV was effective in preventing dermonecrosis.

316. *Bothrops lanceolatus* Bites: Review of the Martinican Experience and Guidelines for Antidotal Treatment

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Objective: Approximately 20–30 cases of snakebite occur each year in Martinique. *Bothrops lanceolatus*, a member of the *Crotalidae* family, notoriously called "Fer-de-lance", is considered to be the only snake involved on this French Caribbean island, with an increasing incidence.[1] Based on our experience, our purpose was to assess envenomation severity and highlight the latest achievements in the treatment of *Bothrops lanceolatus* snakebite. *Methods:* A PUBMED research was undertaken using the terms: *Bothrops lanceolatus*, Fer-de-lance pit viper, *Bothrops caribbaeus*, polyvalent, Bothrofav antivenom, Safety, Snake bites, Martinique; relevant articles were reviewed. *Results:* Envenomation features include the presence of one or more fang marks, localized pain, bleeding from punctures, ecchymosis, and swelling. Thrombocytopenia (70%) and disseminated intravascular coagulation (50%) are frequently observed. Severe cases present with systemic thromboses (including pulmonary, cerebral, and myocardial infarctions), disseminated coagulopathies, and thrombotic microangiopathy. The antivenom therapy (Bothrofav®, Pasteur-Mérieux Connaught) for toxin neutralization appears to be the only effective treatment to prevent severe bite consequences, if intravenously infused early. Antivenom serum is obtained from hyperimmunized horses with *B. lanceolatus* venoms. It contains antivenom F(ab)2 (bivalent antigen-binding fragment, 97%) and Fab (antigen-binding fragment, 3%). Its regimen should be adapted to the envenomation severity. Antivenom therapy was first administered in 1993 in Martinique. In our experience, its effectiveness appeared to be a function of how rapidly it was administrated: in 70 patients who received the antivenom therapy within 6 h of being bitten, no thrombotic

complication was observed. In contrast, 14/33 (42%) patients who received the serum at >8 h after being bitten or who never received it, developed severe thrombotic complications. Consistently, 4/14 (29%) patients who were not treated, died. Only immediate and temporary undesirable reactions were observed, including rash, pruritus, vomiting, and mild bronchospasm. *Conclusions:* Bothrofav is safe and effective to treat *Bothrops lanceolatus* bite if used within 6 hours of being bitten. *Reference:* 1. Thomas L. Thrombotic stroke following snake bites by the "fer-de-Lance" *Bothrops lanceolatus* in Martinique despite antivenom treatment: a report of three recent cases. Toxicon 2006; 48:23–8.

317. Medical Consequences of the Asian Black Hornet Invasion in Southwestern France

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Objective: Introduction of the Asian black hornet *Vespa velutina nigrithorax* into Southwestern France was discovered in 2005.[1] Because of its large size *Vespa velutina* is intimidating and the French media compared the introduction of this stinging insect to the killer-bee problem in America. The medical literature indicates that in comparison with other Asian hornets' species *Vespa velutina* is not considered as a major health threat in Asia. The purpose of this study is to evaluate the actual threat based on experience with hymenoptera stings at poison control centers in France. *Methods:* Since the offending hymenoptera species cannot be identified in most cases, all cases involving hymenoptera stings recorded at French Poison Control Centers from the beginning of 2004 to the end of 2008 were included. Data obtained before and after invasion by the Asian species were compared to check if the presence of the new species had led to an increase in the number of hymenoptera stings in the affected departments. *Results:* A review of data from French poison control centers showed only one envenomation clearly linked to *Vespa velutina*. The victim developed severe symptoms with neuralgic sequelae after being stung 12 times on the head. This case demonstrates that, like the native French hornet species, *Vespa velutina* can be dangerous for man after multiple stings. However, the experience of poison control centers in France shows that the increase of this hornet population in the southwestern regions has not been correlated with an increase in the number of hymenoptera stings in general (study of 824 cases of hymenoptera stings collected in the concerned area by French Poison Control Centers between 2004 and 2008: stability in the incidence of stings before and after Asian hornet invasion in all the 20 concerned French departments). *Conclusion:* These reassuring findings are in agreement with those reported by entomologists from the National Museum of Natural History which has been observing this newcomer since its introduction. *Reference:* 1. Villemant C, Haxaire J, Streito JC. Premier bilan de l'invasion de Vespa velutina en France. Bull Soc Entomol Fr 2006; 111:447–50.

318. Acute Intoxications by Plants: The Moroccan Poison Control Centre Experience

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Objective: The present retrospective study aims to investigate the data of the Moroccan Poison Control Centre (MPCC) in order to describe acute intoxications by plants. *Methods:* Plant poisoning cases were received by telephone or by intoxication reporting forms from hospitals sent to the MPCC between 1989 and 2007. Demographic features, circumstances, type of plants, management delay after intoxication, symptomatology, severity and outcome were analyzed and correlations between them were prepared. The evaluation of severity was made using the poisoning severity score (PSS)[1] and IPCS age groups were used. *Results:* There were 2271 collected cases during the period of study, which represent 3.01% of all cases received by the centre in the same period. The maximum rate of cases was noted during spring (27.7%). The mean age was 19.85 ± 16.38 years (1 day to 91 years), the sex ratio (male/female) was 0.91 and the oral route was predominant. 66.35% of cases were accidental, followed by suicide (13.5%). Patients presented with moderate signs (grade 2) in 32.2% of cases or severe (grade 3) in 9.8%. The most common plants involved in poisoning were *Atractylis gummefera L.* (14.5%), *Peganum harmala* (11.8%), *Datura stramonium* (7.8%) and *Ricinus communis* (3%). Mortality was 6.2%. *Conclusion:* It could be concluded that plant poisoning in Morocco is serious and a prevention strategy is needed. *References:* 1. Persson HE, Sjöberg GK, Haines JA, et al. Poisoning Severity Score. Grading of Acute Poisoning. Clin Toxicol 1998; 36:205–13.

319. The Evaluation of Mushroom-Related Inquiries to the New Zealand National Poisons Centre Between 2004 and 2008

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Objective: The aim of this study was to evaluate human mushroom-related inquiries to the NPC over a 5 year period. *Methods:* A retrospective analysis of all human mushroom-related inquiries to the New Zealand National Poisons Centre (NPC) was undertaken for the years 2004 to 2008. *Results:* The NPC received a total of 950 calls requesting information following human exposure to mushrooms. Of these inquiries, about 73% involved children (less than 7 years of age), 26% involved adults and the remainder was of unknown age. The majority of calls was associated with mushrooms that were not identified (n = 768) followed by puffballs (n = 88) and magic mushrooms (n = 55). Other identified mushrooms included *Amanita muscaria* (n = 28), *Amanita phalloides* (n = 5), *Clitocybe* (n = 1), *Coprinus* (n = 1), cyclopeptide (n = 1), goldtops (n = 2) and *Psathyrella candolleana* (n = 1). Exposures were either child exploratory (73%), unintentional (21%), self harm (4%) or unknown (2%). Most exposure calls concerned ingestion of mushrooms (97%), followed by skin contact (2%) and inhalation (1%). Exposure to magic mushrooms was most significant amongst teenagers age 16 to 18 years. *Conclusion:* Most inquiries received involved children ingesting unidentified mushrooms. Human exposures to magic mushrooms predominantly involved teenagers, using them for recreational purposes.

320. Analysis of Biochemical Indicators of Toxic Liver Injury in Patients Admitted to the Clinic of Occupational Diseases and Toxicology with *Amanita phalloides* poisoning

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Objective: Analysis of selected biochemical indicators of liver injury and evaluation of mycological tests in patients admitted to the Clinic of Occupational Diseases and Toxicology. *Methods:* 19 patients who developed acute liver injury after *Amanita phalloides* ingestion were selected among the patients admitted to the Toxicology Ward during period 1997–2008, 11 women and 8 men, aged between 24 and 84 years. All of them underwent medical examination, mycological and laboratory tests including identification of spores, full blood count, liver and renal function tests. *Results:* Mean age of patients was 55.5±19 years, mean hospital stay of 12±3 days and mean interval between time of ingestion and development of clinical symptoms of poisoning 9 hours 50 minutes, respectively. We observed increased ALT and AST levels after the second day, with maximal values after approximately 72 hours: mean ALT - 5110IU/L and AST - 4120 IU/L, respectively. The prothrombin index started to decrease on the second day, with the minimal PT index dropping to a medium value 36%, during 3th-4th day after the ingestion. We failed to identify the presence of *Amanita phalloides* spores in faeces samples from any patient, however in two cases food remains contained them. *Conclusion: Amanita phalloides* poisoning can be diagnosed clinically on the basis of the significant increase in AST and ALT value and decrease in prothrombin index as well. Mycological tests, in turn, appeared of low diagnostic significance. Results presented indicate the crucial role of regular evaluation of the above mentioned parameters in diagnosis and monitoring the course of *Amanita phalloides* intoxication, whereas identification of spores appeared to be of low diagnostic value.[1,2] *References:* 1. Giannini L, Vannacci A, Missanelli A, et al. Amatoxin poisoning: a 15 year retrospective analysis and follow-up evaluation of 105 patients. Clin Toxicol Liver 2002; 22:78–80. 2. Mas A. Mushrooms, amatoxins and liver. J Hepatol 2005; 42:166–9.

321. 'Natural' Means Safe, Doesn't it?

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Background: The ready availability of so-called natural remedies from Internet websites, together with mostly unsubstantiated claims as to their efficacy in treating various medical conditions, continues to give rise to serious safety concerns. Although the possibility of acute cyanide toxicity from ingestion of large quantities of apricot kernels is well documented, certain websites are still advocating this practice as a 'natural' treatment for cancer - even recommending consumption of 50 kernels daily. *Case report:* A 48 year-old non-smoking female patient attended the emergency department complaining of nausea, headache, abdominal pain and diarrhoea. She was previously diagnosed with multiple endocrine neoplasia (type IIa) and had undergone a number of neck operations including recent removal of a medullary carcinoma of the thyroid. In an attempt to prevent further recurrence of her disease she had taken advice from a website advocating apricot kernel therapy. Initially she had been ingesting 10 kernels/day but this had been increased to 40/day for the past week. She described having a terrible taste since commencing the therapy and that she now felt very unwell and 'raw inside'. Examination revealed mild dehydration and an elevated plasma calcium concentration (2.85 mmol/L). Blood cyanide concentration was normal but her serum thiocyanate concentration was 22.6 mg/L (1–4 mg/L in non-smokers), a level consistent with that found in studies of patients ingesting 1500 mg amygdalin (the cyanogenic component of apricot kernels) daily. Following supportive care and intravenous fluids, her symptoms abated and she was discharged. *Discussion:* Analytical data provided by the Food Standards Agency indicate that bitter apricot kernels on sale in health shops in the UK contain on average 0.5 mg of cyanide per kernel. This patient may therefore have been ingesting approximately 330 microgram/kg cyanide daily - uncomfortably close to the lower acute lethal dose limit in humans of 500 microgram/kg and 28 times the TDI (Tolerable Daily Intake) of 12 microgram/kg/day set by the WHO in 2003. Individuals desperately seeking relief from serious and chronic medical conditions are particularly vulnerable to the exaggerated claims of dangerously irresponsible Internet advertisers and may well find themselves in potentially life-threatening situations. Is there a need for regulation?

322. Identity and Health Risks of Mothball Usage in Greater Accra, Ghana

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Objective: A prior study evaluating the risk factors for poisoning in Greater Accra identified the internal use of "camphor" as a potential public health concern.[1] Twenty-four per cent of community (lay-person) interviewees reported using "camphor" (mothballs) to purify water for drinking and bathing. Physicians in the survey reported cases of hemolytic anemia after mothball ingestion to self-treat stomach-ache, measles, and diarrhea. Since hemolysis is uncharacteristic of camphor ingestion, we sought to identify the actual toxins being sold as mothballs in Greater Accra and use this information to help educate both clinicians and the public. *Methods:* Mothballs are commonly sold by street and marketplace vendors in unmarked saran-wrapped packs. Fifteen small packs of mothballs were purchased from random vendors in three major markets and 6 roadside stands in Greater Accra. All samples were subjected to the float test, which rapidly distinguishes camphor, naphthalene and paradichlorobenzene.[2] One sample was confirmed by the department of health laboratory. *Results:* All samples sank in tap water but floated in a saturated salt solution, consistent with naphthalene. The analyzed sample was positively identified as naphthalene. *Conclusion:* Naphthalene was the ingredient in all the mothballs purchased for the study. Naphthalene is poorly soluble in water, and "camphor water" is unlikely to cause harm. However, ideas about the efficacy of "camphor" as a purification tool may lead to therapeutic misuse by analogy. A high prevalence of G6PD in the Ghanaian population may increase the risk of toxic effects from ingestion of mothballs. Mothballs known in Greater Accra as "camphor" are predominantly naphthalene. A public awareness campaign about the health risks of mothball ingestion is suggested. *References:* 1. Soghoian SE, Clarke E, Nignpense E, et al. Health-seeking behavior after unintentional poisoning in Greater Accra (abstract). Clin Tox 2009; 47:705–6. 2. Koyama K, Yamashita M, Ogura Y, et al. A simple test for mothball component differentiation using water and a saturated solution of table salt: its utilization for poison information service. Vet Hum Toxicol 1991; 33:425–7.

323. Melanotan - a Skin-tanning Product with Potentially Harmful Effects. A Case Series

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Objective: Melanotan is a synthetic hormone, which imitates the natural hormone alfa-MSH. It stimulates skin pigmentation and is used as a tanning agent. Melanotan is not a registered drug but can be bought via the Internet. Several websites show all the "positive" effects including anorexia and increased libido. It is administered subcutaneously. There have been several inquiries to the poisons centre about side effects due to melanotan, and the method of administration is of particular concern and may be associated with risk in the unskilled patient/person. Also the long-term side effects are unknown. *Case series:* Case A: A 23 y/o woman contacted her general practitioner after injecting Melanotan subcutaneously. She had bought the drug from a friend and injected the recommended dose into the abdomen herself after which she developed a haematoma. She was afraid that it could be cancer. Case B: An 18 y/o woman with a history of alcohol abuse and episodes of hyperventilation saw her general practitioner. For the last 2 weeks she has been injecting herself subcutaneously with Melanotan in order to get a tan. After one week's use, she felt she was hyperventilating and had palpitations of the heart. The following week she felt poorly but continued the use of Melanotan. After 2 weeks she began to feel scared and contacted her doctor who, however, could not find any signs of cardiac or respiratory illness. Case C: A 21 y/o man was admitted to the emergency room at 6 am. At 9 pm the preceding evening he had injected himself with Melanotan subcutaneously in the abdomen. Ever since the injection he had felt poorly with nausea and abdominal pain. He had difficulty in breathing, dizziness and a tingling sensation in both arms. After observation for a few hours, he was discharged without further intervention and he did not return to the emergency room. *Conclusion:* Melanotan is used as a skin-tanning product but the full extent of use is presently unknown. The initial adverse effects seem to be mild but we are concerned about the method of administration and the possible long-term adverse effects.

324. Argyria Caused By Homemade Silver Colloid

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Objective: We present a case of silver toxicity caused by homemade silver colloid and a review of the literature. *Case report:* 48 year old man who complained of skin discoloration and neuropsychiatric symptoms presented to our outpatient clinic. He reported ingesting over a 5-year period silver colloid to prevent recurrent lung infections. He stated that after an Internet search into lung infection, he found instructions on how to build a machine to make silver colloid and how often to ingest it to prevent infection. A friend noted the skin changes approximately 4 years after initial ingestion. Besides the skin discoloration, the patient complained of confusion, decreased concentration, tremors, and increasing irritability, interfering with his quality of life and that had continued despite no longer ingesting the silver colloid. *Conclusion:* Silver exposure is through occupational or hobby exposure, as well as medical uses for wound care and indwelling medical devices.[1] Silver toxicity presents mainly as argyria, a blue-grey discoloration of the skin, primarily over the sun-exposed area of the body.[2] Neurologic toxicity from silver is ill defined and described in animal studies.[1] There are two case reports of seizures associated with silver toxicity.[3,4] *References:* 1. Lansdown AB. Critical observations on the neurotoxicity of silver. Crit Rev Toxicol 2007; 37:237–50. 2. Drake PL, Hazelwood KJ. Exposure-related health effects of silver and silver compounds: a review. Ann Occup Hyg 2005; 49:575–85. 3. Mirsattari SM, Hammond RR, Sharpe MD, et al. Myoclonic status epilepticus following repeated oral ingestion of colloidal silver. Neurology 2004; 62:1408–10. 4. Ohbo Y, Fukuzako H, Takeuchi K, et al. Argyria and convulsive seizures caused by ingestion of silver in a patient with schizophrenia. Psychiatry Clin Neurosci 1996; 50:89–90.

325. Acute Hemolysis Following the Extravasation of an Intravenous Phosphatidylcholine Product

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Objective: To present a case series of hemolysis that developed after infusion therapy with phosphatidylcholine administered for lipid exchange therapy. *Case series:* Seven patients received intravenous infusions from vials containing "phosphatidylcholine (100 mg/mL)." The alternative medicine indications were hypercholesterolemias and atherosclerosis, hypertension, and back pain. The compounded formulation was intended for subcutaneous not the intravenous route. Reportedly, the difference in the subcutaneous formulation was riboflavin. The product was diluted in dextrose solution and administered over one hour. All patients developed infusion site pain. Three patients who developed infiltrations also developed acute hemolysis requiring hospitalization. Severity appeared related to the degree of infiltration and/or dose given in these hospitalized patients. Two patients received 2.0 and 2.1 grams, while one patient got 3.0 grams. Two patients did receive the full 3.0 gram dose without infiltration and did not report hemolysis. Symptoms included abdominal pain, diarrhea, sharp chest pain, sweating, chills, myalgias and fatigue. Skin color changes evolved in two patients; presenting pale, becoming red, and then bronze. These two patients presented with brown/black urine with hematocrits falling from 41.2 to 36.2 and 41.0 to 34.0 in the first day. Presenting AST levels ranged from 94 to 113 IU/L in all hospitalized patients, but fell subsequently. One patient had an LDH test elevated at 493. The haptoglobin level of this patient was low, 20 mg/dL (normal; 34–200). Serum total bilirubin levels peaked at 0.9 to 1.8 mg/dL. Despite IVF administration, one patient's serum creatinine rose from 1.8 to 3.1 mg/dL, another's increased from 1.8 to 7.8 mg/dL, but did not require hemodialysis. This patient developed painful left knee swelling. Mydriasis with blurred vision developed. One patient developed acute narrow angle glaucoma, requiring surgical intervention. Testing of the pharmaceutical product ruled out pesticide and metal contamination. The FDA developed a qualitative assay using technical grade phosphatidylcholine. An LC/MS assay confirmed the presence of phosphatidycholine in vials from the lot administered to the patients. Hospitalized patients were treated with intravenous fluids, but no other specific therapies for the hemolysis were needed. *Conclusion:* Infusions with phosphatidylcholine products may cause acute hemolysis.

326. Fulminant Hepatic Failure From Usnic Acid Containing Supplements

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Objective: Complementary and alternative medicine use continues to rise despite limited proof of safety or efficacy. In the US, regulatory action can only occur following demonstrable evidence of harm. We report a case of fulminant hepatic failure in a patient taking two supplements containing usnic acid. Usnic acid, produced in lichen species of the genus *Usnea*, uncouples oxidative phosphorylation and is used in some weight loss formulations as a "fat burner". *Case report:* A 26 year-old woman presented to the hospital with altered mental status and generalized weakness for one day. She denied nausea, vomiting, fever, abdominal pain, or headache. She had no past medical history and was on no prescription medications. She was an amateur bodybuilder and had been taking non-prescription supplements advertised to increase muscle mass for the prior month. On examination she had normal vital signs, reactive pupils, scleral icterus, mild right upper quadrant abdominal tenderness, and no hepatosplenomegaly. Her skin was jaundiced. She was lethargic, but able to answer questions appropriately when aroused, and she had diffuse muscular weakness. A brain CT scan was normal. Blood chemistries included aspartate aminotransferase, 2430 IU/L; alanine aminotransferase, 3252 IU/L; total bilirubin, > 342 µmol/L (direct fraction > 171 µmol/L); INR, 3.7. Her paracetamol concentration and viral hepatitis serologies were negative. She was admitted to the MICU where N-acetylcysteine, continuous veno-venous hemofiltration, and infusion of fresh frozen plasma were unable to improve her clinical status. The patient underwent liver transplantation the following day. Her post-operative course was uneventful and her liver function normalized. Pathology of the liver demonstrated massive hepatic necrosis accompanied by prominent ductular proliferation with minimal inflammatory reactivity consistent with drug-induced hepatotoxicity. *Conclusion:* Usnic acid containing supplements were associated with hepatotoxicity in sixteen published cases. Four of these patients developed fulminant hepatic failure, with three undergoing liver transplantation. The majority of these patients were young with few comorbidities. Risk factors for progression to FHF are unclear, and further investigation of the risk:benefit ratio of this supplement is required.

327. Ethylene Glycol Toxicity in Companion Animals

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Objective: Ethylene glycol is always amongst the ten most common agents implicated in cases with fatal outcomes reported to the Veterinary Poisons Information Service (VPIS) annually. Its toxicity is well documented and treatment is acknowledged to be difficult for many small veterinary outlets. This study aims to evaluate the frequency, morbidity and mortality of ethylene glycol exposures in companion animals. *Methods:* The VPIS database holds case details taken contemporaneously, as well as further information on case progression and outcome collected via postal follow-up. We undertook a retrospective review of all case data for ethylene glycol exposures in cats and dogs from 1991 to date. *Results:* Ethylene glycol exposure was reported in 186 cats and 143 dogs; full follow-up information was available for 84 and 52 cases respectively. Sixteen dogs remained asymptomatic post enquiry, but only 1 cat. Vomiting was reported in 18 canine cases (50%), the most common canine clinical effect, and in 20 (24%) feline cases. Ataxia, convulsions and renal failure were all reported in 7 cases (19%) in dogs. In cats ataxia was seen in 25 (30%) of cases and convulsions in 23 (28%). Renal failure was the most common clinical effect reported in cats occurring in 39 cases (47%); hypocalcaemia was present in 30 exposures (36%). One dog died and 11 were euthanased; only 1 received treatment with IV ethanol. There were 16 deaths (19%) reported in cats and 54 cases euthanased (64%); of these 15 received oral or IV ethanol. *Conclusion:* Our findings indicate that although ethylene glycol ingestions are relatively uncommon the effects of ingestion are severe and frequently result in fatality. Canine exposures are usually witnessed allowing prompt and successful intervention; the mortality rate in our study ranging between 8.4–23.1% of all cases referred. In the more independent cat, diagnosis is more complicated without circumstantial evidence; they may groom off contaminated fur, but malicious intent is commonly suspected. Successful veterinary intervention is rarely possible with late presentations, and prognosis is poor (a mortality rate between 37.6–83.3% indicated by our data) even with heroic and costly measures.

328. Effect of Risk-Reducing Actions on Metaldehyde Intoxications by Dogs

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Objective: Metaldehyde is the ingredient of most molluscicide preparations. It can be quite attractive to dogs. Severe intoxications frequently result in continuous convulsions and deaths. To diminish the number of these intoxications a number of actions were initiated in December 2007 by the federal authorities. We report the effects of these actions by comparing calls to the poison center concerning metaldehyde poisonings two years before and after the start of these actions. *Methods:* The actions included control of the Bitrex concentration as previous tests showed little or no Bitrex at all in some of the samples, adjusted instructions for use on the label (e.g. number of granules/m^2 instead of grams/100 m^2) and distribution of a leaflet stating the correct use of these products. *Results:* For the two years before and after the start of the actions we looked for major symptoms and more specifically convulsions at the time of the call. We did not look for the number of deaths because the poison control centre is only rarely contacted in case of the death of a dog. As can be seen in the table (Table 1) no apparent amelioration was observed. Compared with the two years before the start of the actions there were more calls and more major symptoms (with or without convulsions) in the two years after (Table 1). *Conclusion:* Risk-reducing actions like the ones described above do not diminish the number of serious metaldehyde intoxications in dogs. Other measures are necessary if a reduction in these kinds of intoxications is needed.

Table 1. Major symptoms and convulsions in dogs intoxicated with metaldehyde 2006–2009

Year	# dogs intoxicated	Major symptoms (%)	+ Convulsions (%)
2006	27	10 (37)	7 (26)
2007	56	8 (14)	7 (13)
2008	53	16 (30)	12 (23)
2009	39	12 (31)	9 (23)

329. Chlormethiazole Poisonings in Dogs - The First Case Report

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Objective: Chlormethiazole is an anticonvulsive and sedative-hypnotic drug. In Sweden it is used mainly in geriatrics and for treatment of withdrawal symptoms after alcohol abuse. The mechanism of action is not fully understood, but chlormethiazole probably potentiates the GABA transmission and enhances a unique glycine-mediated inhibition of electrical stimuli within the central nervous system. A few experimental studies of chlormethiazole in dogs have been published in the literature but poisonings have not previously been described. According to information from the manufacturer no domestic animal poisonings have been noted. Since 1999, the Swedish poisons centre has been consulted regarding twelve cases of chlormethiazole ingestion in dogs. Eleven of these showed none or only mild symptoms, and one case experienced more severe symptoms and will be presented here. *Case report:* In the afternoon, at 4 pm, a 10-year-old (8 kg) male Border Terrier ate 10–15 capsules containing 300 mg chlormethiazole each. The dose ingested corresponds to 3000–4500 mg or 375–563 mg/kg. After approximately one hour, the dog was brought to an animal hospital. The Border Terrier was unconscious, had seizures, tachycardia of 170/min and weak, irregular pulse. Furthermore, it also presented with breathing difficulties, tachypnoea, hypersalivation and red-greyish mucous membranes. A dose of 4 mg diazepam was given intravenously with prompt effect on the seizures. Oxygen was administered as well. Laboratory values showed no evident alterations. After examination at the emergency department the dog was transferred to the intensive care unit. The dog then had more pronounced breathing difficulties, cyanosis was evident and the saturation was only 63%. The heart rate had increased to 193/min with a blood pressure of 130 mmHg systolic. The dog was intubated and the saturation improved but still remained a little low, 93%. Despite an improved state the owner later decided to euthanize the dog. *Conclusion:* According to our knowledge this is the first severe canine poisoning case after chlormethiazole ingestion.

330. Hydrofluoric Acid - Experiences of 157 Exposures 2003–2008

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Objective: Hydrofluoric acid (HF) is an extremely toxic chemical used exclusively in work place settings in Sweden. Even minor dermal exposures are normally managed in hospital. *Methods:* We prospectively compiled available data regarding consultations after HF exposures to our centre 2003–2008. *Results:* During the 6-year period, 157 cases were included. All victims were adults and 84% were male. At least 126 cases received hospital care. The type of exposure was classified as dermal in 68%, inhalation in 16%, eye in 6%, ingestion in one case, and mixed in 10%. The concentration of the HF was <30% in 86 cases, >30% in 27, and unknown in 44. Among the victims with dermal involvement (121 cases), 96 had suffered a minor dermal exposure (i.e. an area corresponding to <1% of the body surface) without risk for systemic toxicity, 16 had been exposed to an area equivalent to 1–5%, and five to an area >5% of the body surface. The size of the exposed area was uncertain in four cases. The maximum symptomatology of all 157 cases was retrospectively graded according to the poisoning severity score (PSS) as follows; PSS 0 (no symptoms) in 33 cases (22%), PSS 1 (mild) in 106 (69%), PSS 2 (moderate) in three, and unclear in 15 cases. Considering treatment, 86 of the 121 victims with dermal involvement were flushed immediately, 16 were flushed later, and for the remaining 19 flushing-data was unavailable. Eighty cases were also treated with 2.5% calcium gluconate gel, of which 33 received calcium gel at the site of the incident. Among the total study population, calcium was administered orally in four cases, subcutaneously in three, intravenously in seven, as nebulization in six, and intra-arterially in one case. Of the 96 cases with minor dermal exposure, 70 had performed immediate flushing and 53 had received topical calcium gel as well. Among the latter 70 cases, none had a PSS >1. *Conclusion:* Based on these findings, we propose that, irrespective of HF concentration, minor dermal exposures may be safely managed out of hospital if immediate water flushing and application of calcium gel have been performed.

331. Phosgene Exposure with Severe Pulmonary Edema - Use of Beclometasone Spray as Preventive Measure

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Objective: Phosgene is an important precursor for the production of polyurethanes and polycarbonates. Whereas the chemical industry is using phosgene on demand without storage, in smaller laboratories triphosgene, a dry chemical, is used to create phosgene for chlorination. *Case report:* A student was supervising when triphosgene was heated with a catalyst producing phosgene for chlorination. A glass grinding hose coupling on a flask with 100 grams of triphosgene was disconnected. The student tried to fix the leakage for several minutes. She left the laboratory due to irritation of eyes, throat and nausea. Her professor went into the laboratory, he stopped the reaction by cooling and connecting the dislocated coupling. Personnel walking in front of the laboratory recognised an odour and burning of their eyes. The building was evacuated; the fire brigade and the toxicological emergency team were activated. Forty persons on the scene received 200 µg of beclometasone by inhalation, and were transported to 4 hospitals with the instruction to stay overnight. The student and the professor refused to take the spray. They arrived, due to police questioning, late in hospital and were treated as outpatients without any signs or symptoms. Twelve hours after the incident the professor and the student developed severe dyspnea and coughing and were brought back to us. They exhibited blood gases under oxygen treatment of 60 mmHg/ SaO_2 87 on admission. Using a CPAP mask the paO_2 was around 80 to 90 mmHg for 48 hours before improvement ensued. Both patients showed inflammatory signs, peaking on day 2. At admission signs of hemoconcentration were present. The thorax x-ray revealed pulmonary edema on both sides in both patients. The body plethysmography resulted in reversible obstruction, restriction and severe hypoxemia during exercise on day 4, on day 10 it was normal. Eight patients were treated in our department with mild irritation of the eyes on-site. All had received beclometasone spray. None developed pulmonary injury. *Conclusion:* Pulmonary edema after short phosgene exposure developed with a long latency. Hospitalisation of all exposed persons seems advisable. Beclometasone inhalation may prevent pulmonary oedema though only patients with mild exposure were treated.

332. Respiratory and Skin Disorders Associated with Disaster Victim Identification in the Aftermath of the 2004 Southeast Asia Tsunami

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Objective: Reports on health problems after the Southeast Asia tsunami in 2004 have focused on mental health and infectious diseases.[1,2] An association between airway problems and exposure to disinfectants and formaldehyde was first reported in Swedish disaster victim identification (DVI) personnel.[3] As a consequence Danish personnel have been examined in order to identify health disorders associated with DVI work in Thailand, focusing on chemical exposure. *Methods:* A two-step strategy with screening by a questionnaire followed by clinical examinations of screen positive was followed. Respiratory symptoms were evaluated with pulmonary-function and skin-prick test; skin disorders were evaluated clinically and by patch test. Association with DVI work was assessed using temporality and plausibility as criteria. *Results:* Valid questionnaires were returned from 152 of 165 persons (92%) having worked in Danish DVI teams. Thirty of these were screen positive and 23 accepted the invitation for clinical examinations, 10 with asthma/ rhinitis, 7 with dermatological disorders, 2 with both respiratory and skin disorders and 4 with other or no disease. The association with DVI work was assessed as probable for two cases of contact dermatitis and possible for two cases of asthma and two with other skin disorders. For one person a two-year lasting deterioration of pre-existing asthma and for another a lasting exacerbation of an allergic contact dermatitis were established. All other disorders were considered unrelated to DVI work. *Conclusions:* Skin and respiratory disorders associated with DVI work were found in 8 of 152 persons (5%) who had worked in the catastrophe area. A routine follow-up is recommended for future similar situations. *References:* 1. Thoresen S, Tønnesen A, Lindgaard CV, et al. Stressful but rewarding: Norwegian personnel mobilised for the 2004 tsunami disaster. Disasters 2009; 33:353–68. 2. Jeremijenko A, McLaws ML, Kosasih H. A tsunami related tetanus epidemic in Aceh, Indonesia. Asia Pac J Public Health 2007; 19:40–4. 3. Melkas S, Svartengren K, Nordquist E, et al. Hög exponering för luftvägsirriterande ämnen vid identifiering av tsunamioffer. Läkartidningen 2008; 105:1296–9.

333. Delayed Oral Complications of Mustard Gas Poisoning in Iranian Toxic Veterans Referred to the Oral Medicine Department of Mashhad Dental Faculty

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Background: The effects of chemical gases on tissue exposed to the environment (skin, airways and eyes) depends on the amount of poison and duration of contact and some areas such as skin folds and parts with thin epidermis are more sensitive to gases. Considering the importance of oral lesions in evaluation and treatment in toxic veterans and since non keratinized mucosa of the larynx (of which involvement has been reported in studies on airways of veterans) are histologically similar to some of the oral regions such as soft palate and floor of the mouth, this study was conducted to determine the delayed oral complications of mustard gas poisoning in toxic veterans referred to the Oral Medicine Department of Mashhad Dental Faculty. *Methods:* In this descriptive cross sectional study, 37 of the toxic veterans referred to the Oral Medicine Department of Mashhad Dental Faculty, were orally examined during a six month period in 2009. The patients' data including demographic data, duration of oral lesion presence, history of medications, the type of chemical gas involved and disability percentage were recorded. The data were descriptively assessed through SPSS statistical software. *Results:* Among the 37 veterans referred, all patients had oral soft tissue lesions. The most common findings were xerostomia, mucositis, candidiasis, gingivitis and periodontitis respectively. *Conclusion:* Presence of highly frequent oral soft tissue lesions in Iranian toxic veterans compared to the general population necessitates periodic oral soft tissue examinations by oral medicine specialists.

334. Contact Dermatitis to Dimethylfumarate: 27 Cases

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Objective: Dimethylfumarate (DMFu) has been used as a biocide for the preservation of furniture and clothing in Southeast Asia. Numerous cases of severe contact dermatitis have been reported in France and several other European Union states. This study analyzed the cases reported to the Paris Poison and Toxicovigilance Centre (PPTC). *Methods:* Each patient notifying suspected exposure to DMFu to PPTC was invited to attend a medical examination and patch testing with the European standard battery, DMFu (0.01% in petrolatum and in water), and, when possible, with the suspected item. Following these investigations, causality was evaluated according to the French causality method for pharmacovigilance. *Results:* Fifty-seven symptomatic cases of suspected exposure to DMFu were notified to PPTC up to 10.31.2009. Only 27 patients could be examined and 25 were patch-tested. The suspected sources of exposure were seating, shoes or boots, and clothes in 9, 16 and 2 cases, respectively. Clinical examination was performed several weeks after the end of the exposure in most cases. Ten patients who were asymptomatic at examination reported skin lesions topographically and chronologically related to exposure to the suspected item in 7 and 5 cases, respectively. The other 17 patients still presented an erythematosquamous rash, which was mild in most cases; skin lesions were topographically suggestive of contact dermatitis to the suspected source in 14/17 cases and were chronologically linked to exposure in 12 of these 14 cases. Patch-tests with DMFu and/or the suspected items were carried out in 25/27 and 16/27 patients, respectively, and were positive in 9/25 and 8/16 cases. Contact dermatitis to a DMFu-treated item was estimated to be likely in 17 cases, possible in 4 and dubious in 6 cases. *Conclusion:* Since 2006, numerous cases of contact dermatitis to DMFu-treated items have been observed in the EU. We report one of the largest series. In all of these cases and in previous reports, the sources of exposure were seats, shoes or clothes imported from China. Our cases and a review of literature establish that DMFu may be responsible for both irritative and allergic contact dermatitis.

335. Caustic Burns of the Oesophagus: Experimental Evaluation of an Amphoteric Agent in a Goat Model

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Objective: Currently, no effective cure for caustic oesophageal burns exists. Amphoteric concept and hypertonicity have previously been used for active decontamination of cutaneous/ocular chemical burns. This study evaluated its efficacy (as a gel) on sodium hydroxide oesophageal lesions. *Methods:* All applicable animal use guidelines were followed. The experiment was performed on two groups of 5 anesthetized goats each. In the first, acute toxicity was studied with a high gel excess. In the other, efficacy was evaluated. After surgical cervicotomy, the oesophagus was opened and laid out flat for a 10 cm length. 50 µL of sodium hydroxide (5M) were deposited by spots, during different times of contact, alone or followed by gel application. Macroscopic lesions on mucosa and muscularis, and its pH (during 30 min with gel exposure) were evaluated. Anatomopathologic analysis supplemented the study. *Results:* In less than 3 minutes, mucosal lesions appeared. Sodium hydroxide diffuses and reaches the muscularis after 12–13 minutes. Severe injury (stage III) appeared macroscopically after approximately 30 minutes. Administration of an excessive dose of gel orally was consistently associated with diarrhea. Administered early after 5 and 10 minutes, the gel prevented the diffusion of sodium hydroxide into the muscularis and integrally preserved it. Beyond 20 minutes, the muscularis was already damaged. The gel blocked the extent of tissue destruction on macroscopic, pH-metric, and histological assessments. *Conclusion:* The amphoteric and hypertonic gel appears advantageous for decontamination of oesophageal caustic burns. Administered very early, it prevented the development of serious lesions in this animal model; beyond 20 min, its effectiveness was lessened. This is in agreement with a previous study performed in a pig model. Based on these data, the gel is promising for further evaluation. Human trials could be proposed once the innocuousness of the gel by this administration route has been completely evaluated.

336. Neutropenia and Cardiac Enzyme Elevation Following Inhalational Aluminium Phosphide Exposure

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Objective: Aluminium phosphide poisoning is relatively uncommon in the United Kingdom although mortality is high.[1] Toxicity is mediated through the release of phosphine gas following reaction with water or (stomach) acid and leads to mitochondrial failure.[1] Here we present a case report of inhalational aluminium phosphide toxicity that is unusual due to the development of marked leucopenia and elevated cardiac enzymes. Leucopenia and cardiac toxicity are not widely described following exposure by inhalation, as compared to ingestion, although when present leucopenia is said to represent severe toxicity.[2] *Case report:* A previously fit 43 year old female presented to emergency services with a history of having inhaled the fumes generated by placing approximately 60 g of aluminium phosphide pellets into a bowl of water, whilst in an enclosed space in a suicide attempt. She reported significant nausea but no vomiting. Conscious level was normal throughout. Admission blood pressure was 80/50 mmHg and pulse rate 110/min. There was no clinical or radiological evidence of pulmonary oedema with oxygen saturations maintained at 98% on room air. Admission ECG was normal. She remained hypotensive for 48 hours, despite fluid resuscitation, but she maintained her urine output without inotropic support. Her troponin I was elevated at 0.86 µg/L on admission, falling subsequently. The admission white cell count was reduced at on admission 3.4×10^{-9}/L and fell further to 1.3×10^{-9}/L, (neutrophils 0.13×10^{-9}/L), over the next 48 hours, but normalised by day 5. There was no evidence of haemolysis, disseminated intravascular coagulation, acid-base disturbance, renal failure or hepatic dysfunction. By day 6 post overdose there were no ongoing features of toxicity. *Conclusion:* Although well recognised after ingestion, neutropenia and cardiac toxicity are not commonly seen following inhalation, especially in the absence of other features of severe toxicity. Clinicians should be alert to these features after inhalational poisoning. *References:* 1. Proudfoot AT. Aluminium and Zinc phosphide poisoning. Clin Toxicol 2009; 47:89–100. 2. Wahab A, Zaheer MS, Wahab S, et al. Acute aluminium phosphide poisoning: an update. Hong Kong J Emerg Med 2008; 153:152–5.

337. Intentional Ingestion of Concentrated Potassium Chloride Results in Caustic Injury

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Objective: Although ingestion of pharmaceutical potassium can produce hyperkalemia, this case is presented to highlight that non-pharmaceutical potassium salts can also produce severe caustic injury. *Case report:* A 31 year old man presented to the hospital with severe abdominal pain and vomiting after drinking 300 grams of KCl purchased from a scientific supply company 8 hours earlier. Thirty minutes following ingestion, he developed left shoulder and epigastric pain and vomited. Upon presentation he had one episode of hematemesis. Vital signs were: 146/76 mmHg, 95 beats/min, 19 breaths/min, 93% oxygen saturation on RA and a normal temperature. Examination was notable for: limited respiratory effort during breathing due to pain, a rigid abdomen with epigastric tenderness. His electrocardiogram showed peaked t-waves, and serum potassium was 7.5 mEq/L, and a serum lactate of 4.3 mmol/L. A chest radiograph did not reveal free air, but CT scan showed transmural gastric irritation and a small left-sided pleural effusion. The patient's hyperkalemia was treated with insulin, dextrose, calcium, albuterol, furosemide, and saline. A proton-pump inhibitor was given for GI bleeding. WBI was instituted to remove any remaining potassium chloride, and nephrology was consulted in case hemodialysis was required. Upper endoscopy revealed severe hemorrhagic gastritis throughout the stomach including the antrum with areas of eschar. The distal esophagus and duodenum were also involved. He was admitted to the medical ICU for close monitoring. His hospitalization was complicated by the formation of communicating abscesses (from microperforations in the stomach) in the L pleural space and posterior to the stomach. They were drained with pig-tail catheters and treated with antibiotics for GI microorganisms. The patient had a percutaneous jejunostomy tube inserted for nutrition. Three months later, he is still receiving nutrition through the jeunostomy tube and has been admitted to the hospital for fever twice. *Conclusion:* Intentional ingestion of large amounts of potassium chloride produced both hyperkalemia and a severe caustic injury.

338. Comparative Analyses of Chemical Poisonings in the South Caucasus Region

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Objective: The purpose of this joint prospective study was the evaluation and analyses of the characteristics of acute chemical poisoning cases in Azerbaijan and Georgia. *Methods:* This investigation was performed on data for poisoned patients admitted to the Republican Toxicology Center (RTC) in Baku (Azerbaijan) and poisoned patients admitted to hospitals in Tbilisi (Georgia) in 2007. *Results:* There was a total of 1182 hospitalizations in the RTC's intensive care unit and 1646 poisoned patients admitted to hospitals in Tbilisi. The mean lengths of hospitalization were 3.2 days in Azerbaijan and 1.2 days in Georgia. Intoxications were more frequent, as were males (51% in Azerbaijan to 67% in Georgia) and those in the 20–40 age group. Among the pharmaceuticals, poisonings by antiepileptic, sedative-hypnotic and antiparkinsonism drugs (T42) and poisonings by psychotropic drugs (T43) were the most frequent. The other cases of poisonings were inhalation of carbon monoxide (T58) - 173 hospitalizations in Azerbaijan and 77 hospitalizations in Georgia; alcohol poisoning (T51) - 50 admissions in Azerbaijan and 697 admissions in Georgia; poisoning by narcotics and psychodysleptics (T40) - 50 cases in Azerbaijan and 36 cases in Georgia; toxic effect of corrosive substances (T54) 176 patients in Azerbaijan and 56 patients in Georgia; poisoning by pesticides (T60) - 39 patients in Azerbaijan and 11 patients in Georgia; toxic effect of contact with venomous animals (T63) - 70 patients in Azerbaijan and 23 patients in Georgia and toxic effect of other noxious substances eaten as food (T62) - 7 patients in Azerbaijan and 85 patients in Georgia. The mortality rates were 3.1% in Azerbaijan and 0.74% in Georgia. Corrosive liquid poisonings were most often fatal (41% of total mortality) in Azerbaijan and alcohol poisonings were most often fatal (38% of total mortality) in Georgia. *Conclusion:* These data provide information about toxicoepidemiological situation in the South Caucasus countries and could help to develop a joint program of prevention of acute chemical poisonings in this region.

339. Reports on Cases of Fatal Carbon Monoxide Poisoning due to Charcoal Grills Received by The Federal Institute For Risk Assessment in 2009: Background, Principal Measurements and Considerations as to Prevention

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Objective: In the context of compulsory notification of cases of poisoning, The Federal Institute For Risk Assessment (BfR) received eight reports of fatal cases of carbon monoxdide (CO) poisoning after indoor use of charcoal grills in 2009. Two cases resulted in very severe neurological damage. CO is odourless, colourless and non-irritant and therefore, does not produce any warning effect for humans. The gas is lighter than air and readily absorbed through the lungs, which initially remains unnoticed. Insufficient ventilation in indoor environments will quickly result in lethal concentrations of the toxic gas. *Methods:* The cases were investigated and documented at BfR, and assessments of individual cases as well as an analysis of cases reported so far under §16e Chemicals Act were performed. For a better assessment of exposure, the Institute of the Fire Department of Saxony-Anhalt (IdF) performed principal measurements of CO emissions from charcoal products inside a fire container in the context of a research project of the Federal Land of Saxony-Anhalt. *Results:* In all cases, charcoal grills had been improperly operated indoors and probably also been used for heating. Examinations performed by IdF on the dynamics of the development of O_2, CO and CO_2 concentrations have demonstrated the considerable risk posed by open fires in rooms lacking the necessary ventilation. Calculations of the absorbed toxic dose according to the Fractional Effective Dose (FED) model [Purser] have confirmed the fatal risk posed by indoor operation of charcoal grills. Very severe and life-threatening poisoning may occur within 30 minutes. *Conclusion:* Investigations into cases and evaluations of measurements have documented the risk posed by CO formation in indoor environments. The cluster of fatal cases observed in the first half of 2009 has indicated that, obviously, a part of the population is not aware of the risk posed by indoor open fires. Even the use of embers as a source of heat in rooms may cause life-threatening poisoning. Open windows and doors do not provide safety. In cases of moderate to severe poisoning, persons affected will mostly exhibit a cherry-red healthy skin colour. This may lead to misjudgement of the situation, particularly if alcohol has been consumed.

340. A Case of Shoe Dermatitis Resulting from Exposure to Dimethylfumarate

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Objective: To describe a case of contact dermatitis to shoes contaminated with dimethylfumarate (DMF), a biocide used in China to protect exported goods, recently occurred in Italy. *Case report:* On 9 March 2009, a 35 year old woman, while wearing a new pair of shoes for an 8 hour period started to experience feet itching. On the following day, she suffered an increase in feet itching, pain and redness. These reactions were considered to be related to fungal infection and topically treated with antifungal cream. In the subsequent two days the woman experienced feet blistering and swelling limited to the area which was in contact with the shoes. She consulted a general practitioner who considered the observed lesions suggestive of contact dermatitis and prescribed topical application of cortisone. Two days after the beginning of the treatment, the patient developed eczematous second degree burns and referred to a first aid service for medication. Twenty five days after the onset of symptoms, the patient consulted the Poison Control Centre (PCC) of Milan in order to get information on possible shoe allergens. Considering recent reports,[1] a test for the presence of DMF in leather shoes was requested. The analyses performed by using high performance liquid chromatography and capillary gas chromatography quantified an average concentration of 383 mg/kg DMF in the shoes. No patch testing on the patient has been yet been performed. *Conclusion:* In Europe, the Commission Decision 2009/251/EC requires Member States to ensure that products containing DMF are not produced or made available on the market. In accordance with this Decision, the Italian Ministry of Welfare requires that the importers of goods from outside European Countries certify the biocide used to avoid their spoilage or degradation and performs systematic controls in order to verify their composition. Furthermore, a surveillance of cases with exposure to desiccants or with dermatitis of unknown origin referred to the PCCs has been recently implemented. That activity allowed detection of the case of shoe dermatitis reported here and a few other cases which are at the moment under investigation. *References:* 1. Rantanen T. The cause of the Chinese sofa/chair dermatitis epidemic is likely to be contact allergy to dimethylfumarate, a novel potent contact sensitizer. Br J Dermatol 2008; 159:218–21.

341. Poisoning with Poppers. Enquiries Relating to Nitrite Toxicity in the United Kingdom

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Objective: Recreational use of amyl nitrite and related substances (e.g. butyl or isobutyl nitrite) can be associated with serious adverse effects including hypoxia and methaemoglobinaemia. The incidence of toxicity in the UK is not well understood. This information would be useful for planning strategies to minimise harms from nitrite abuse. This project was therefore carried out to quantify episodes of nitrite toxicity in the UK. *Methods:* Accesses to TOXBASE®, the National Poisons Information Service (NPIS) online database were searched for the period 2000 to 2008. NPIS telephone enquiries for 2007 and 2008 were also analysed, with detailed evaluation of 2008 enquiries by manual searching of individual entries. *Results:* TOXBASE®, accesses to nitrites and related entries (e.g. 'poppers', liquid gold etc) increased as a proportion of all TOXBASE®, activity from 0.12% (238 of 188,000 accesses) in 2000 to 0.17% (1664 of 965,000 accesses) in 2008. There were 155 telephone enquiries about alkyl nitrites and related substances, 52 in 2007/8 and 103 in 2008/9, involving 103 males and 49 females. The most common age group involved was 20–30 years (n = 54, 35%). Exposures were most commonly listed as recreational (55%), accidental (23%) or intentional (14%) and were acute in 150 cases (97%). Episodes occurred most commonly in the home or in a domestic setting (65%), in a public area (22%) or at work (3%). Of the 103 episodes reported in

2008/9, there were 17 cases (17%) where either the poison severity score was recorded as 'severe', methylthioninium chloride ('methylene blue') was given or advised or the methaemoglobin concentration was documented as >30%. There was one further patient who experienced a seizure, another who was severely cyanotic and a further 7 who had measured oxygen saturation less than 90%. *Conclusion:* Severe intoxication with nitrites appears uncommon in the UK, although this may be underestimated as in some cases referral to NPIS may not be made or patients may deteriorate after the NPIS enquiry. TOXBASE®, data suggests that incidence of intoxication may be increasing. Further study of telephone data over a longer time period is warranted.