

ABSTRACTS

# Abstracts of the 2012 International Congress of the European Association of Poisons Centres and Clinical Toxicologists, 25 May–1 June 2012, London, UK

## 1. Emergency Triage of the Poisoned Patient: A Toxicology Risk Assessment in 5 Minutes

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**Introduction:** Triage of the patient presenting to the Emergency Department (ED) has evolved considerably over the last two decades. Since its inception, triage systems have continued to develop and be modified into ever more useful tools in early recognition of the acutely ill. Common systems used around the world in triaging emergency patients are the Australasian Triage Scale (ATS) and the Manchester Triage System (MTS). Applying this to the poisoned patient, triage aims to risk stratify a given overdose or envenomation to predict clinical deterioration and potential for complications.

**Discussion:** Since its development in the early 1990s, the ATS has had multiple revisions and improved on earlier issues with inter-rater reliability. The ATS comprises five categories of clinical acuity associated with timeframes for medical attention.<sup>1</sup> The basis for assigning ATS categories rely on Airway, Breathing, Circulation and Disability parameters, involving appropriate matching of clinical descriptors to ATS categories. The subjective nature of ATS category assignment allows for variability in triaging between triage officers. The Canadian Triage & Acuity Scale (CTAS) is similar to the ATS and came into use throughout Canada by 1997. The MTS was introduced in the UK in 1996 and its use is now widespread, particularly in Europe.<sup>2</sup> MTS has an algorithmic approach to ED triage and, by using an array of flowcharts, the triage officer chooses a five-scale triage category for a particular presenting complaint. The more objective nature of the MTS has increased its acceptance in many parts of the world, though alterations to the flowcharts may be required in specific or geographically unique circumstances, such as envenomation.<sup>3</sup> The essential goals of triage are to identify life-threatening conditions, prioritise patients with higher acuity presenting complaints, and instituting early treatment strategies.<sup>4</sup> Overall, triage officers aim to correctly triage ED presentations to match the level of urgency. Under-triage of patients leads to increased risk of potential complications, morbidity and mortality. Over-triage has little consequence for the specific patient, however, affects the ED as a whole by creating stress, increasing workload and delaying treatment for the true high acuity patient. In the case of poisoned patients, emergency triage aims to perform a risk assessment of the overdose or envenoming within 5 minutes. This key function has a major impact on time to medical treatment and risk of adverse outcome. Additionally, in deliberate self-poisoning presentations, the psychiatric background, social stressors, affect and suicidality of the patient all have a significant

bearing on the assigned triage category. The existence of poisons information centres (PIC) within a healthcare system has significant implications on emergency triage presentations.<sup>5</sup> The ability to filter the majority of trivial and minor exposures with out-of-hospital management selects higher acuity patients for ED presentation. PICs also play a key role in ambulance triage at the scene as well as in ambulance control systems that decide on transportation of potentially poisoned patients. ED triage officers may also choose to contact a PIC during or at the completion of triage in order to modify risk stratification. Experienced triage officers are able to appropriately triage poisoned patients with symptoms and signs, particularly those involving agents that cause reduced level of consciousness or coma. Difficulties in triage are more common with the well-looking patient whose toxidrome has yet to develop or does not manifest in altered sensorium, gastrointestinal upset or dyspnoea. Common triage pitfalls include ingestions of cardiac medications, heavy metals, oral hypoglycaemic agents, unusual chemicals, sustained-release preparations and paediatric patients.<sup>6,7</sup> Emergency triage systems, in their current form, do not necessarily take into account a risk assessment of the potential toxicity of the agent ingested. As such, they may fail to predict precipitous clinical deterioration in a minority of cases. Furthermore, failure to recognise potentially severe complications of specific agents, such as calcium channel blockers, may delay early life-saving interventional strategies. The triage officer has an additional role in instituting decontamination, if appropriate. **Conclusion:** Emergency triage of the poisoned patient is a crucial decision point in their medical management – ultimately, it can mean the difference between life and death. Several emergency triage systems are utilised around the world, each with its own limitations in risk assessment. The existence of poisons information centres within a healthcare system has significant bearing on ED presentations of poisoning and envenomation. There are uncommon and dangerous toxicological presentations that require an astute and experienced triage officer to recognise the potential for life-threatening toxicity. **References:** 1. Australasian College for Emergency Medicine. The Australasian Triage Scale. www.acem.org.au [accessed 23 Jan 2012]. 2. Mackway-Jones K, Marsden J, Windle J, eds. Emergency Triage. Manchester Triage Group. 2nd ed. Oxford, England: Blackwell Publishing. BMJ Books, 2005. 3. Grouse AI, Bishop RO, Bannon AM. The Manchester Triage System provides good reliability in an Australian emergency department. Emerg Med J 2009; 26:484–6. 4. Commonwealth of Australia. Emergency Triage Education Kit, 2009. www.health.gov.au [accessed 23 Jan 2012]. 5. Benson BE, Smith CA, McKinney PE, et al. Do poison center triage guidelines affect healthcare facility referrals? J Toxicol Clin Toxicol 2001; 39:433–8. 6. Bartlett D. Tricky toxic presentations at triage. J Emerg Nurs 2005; 31:403–4.

7. Wolf L. Considerations in triage for the intoxicated patient. J Emerg Nurs 2008; 34:272–3.

## 2. The Role of the ECG in Risk Assessment of the Poisoned Patient

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**Background:** Poisoning is the leading cause of cardiac arrest in patients under 40 years of age<sup>1</sup> and the second-leading cause of injury-related fatality across all age groups in the US<sup>2</sup>. The ECG represents a rapidly available clinical tool that can help clinicians manage poisoned patients. Specific myocardial effects of cardiotoxic drugs have well-described electrocardiographic manifestations. The objectives of this review are: (a) to summarize specific toxic effects on the myocardium that can cause characteristic ECG changes; (b) to review the approach to the ECG in acutely poisoned patients and ECG-toxidrome pearls; and (c) to integrate ECG interpretation with management decisions in the poisoned patient. **Discussion:** Clinicians should adopt a systematic approach to ECG interpretation for poisoned patients that includes analysis of rhythm, intervals (QRS, QT, etc), and ischemic changes (ST and T wave changes). Common patterns of ECG manifestations may serve as pearls to aid clinicians in diagnosis and management of poisoning. In the setting of poisoning, drug classes that cause characteristic ECG manifestations include ion channel antagonists (sodium, potassium, calcium), cardioactive steroids (sodium-potassium ATPase), and beta adrenergic antagonists. Recent data suggests that initial ECG interpretation may predict in-hospital prognosis for patients with undifferentiated poisonings in the emergency department.<sup>3</sup> Poisoned patients suffering from cardiac arrest should be treated according to Advanced Cardiac Life Support (ACLS) guidelines with consideration of toxicology-specific antidotes as adjunctive therapy.<sup>4</sup> **Conclusion:** In medical toxicology, the ECG plays an important role in the evaluation of the poisoned patient to identify or exclude cardiotoxicity, as well as to take fundamental initial steps in initial management. A sound understanding of ECG interpretation and the characteristics of cardiotoxicity is necessary to establish a basis for the utility of the ECG in drug overdose. A systematic approach to the ECG in poisoned patients based on patterns of cardiotoxicity may help clinicians identify management strategies to ameliorate cardiotoxicity. **References:** 1. ECC Committee, Subcommittees and Task Forces of the American Heart Association. 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation

2005; 112(24 Suppl):IV1–203. 2. Centers for Disease Control and Prevention (CDC). Increases in age-group-specific injury mortality—United States, 1999–2004. *MMWR Morb Mortal Wkly Rep* 2007; 56:1281–4. 3. Manini AF, Nelson LS, Skolnick AH, et al. Electrocardiographic predictors of adverse cardiovascular events in suspected poisoning. *J Med Toxicol* 2010; 6:106–15. 4. Vanden Hoek TL, Morrison LJ, Shuster M, et al. Part 12: cardiac arrest in special situations: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2010; 122(Suppl 3):S829–61.

### 3. Toxicology Screening in the Immediate Management of the Poisoned Patient – What Do You Really Need and What's Out There? A UK Perspective

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**Objective:** The indications for, and availability of, laboratory assays required for the effective management of the poisoned patient are described. **Methods:** Currently recommended assays, their indications and their availability were reviewed within the United Kingdom by the National Poisons Information Service and the Association for Clinical Biochemistry. **Results:** Laboratory assays for toxins and/or their metabolites are a very important part of the management of patients with potentially serious poisoning. However, there is evidence that laboratory toxicological investigations are overused by medical staff. There is also evidence that the availability of these investigations varies between hospitals, particularly when required outside normal working hours. This may present problems in management. Indications for laboratory assays include: confirmation of the diagnosis of poisoning when this is in doubt; to influence patient management, (e.g. the need for further investigations, antidotes, haemodialysis or other extracorporeal methods of elimination, or to stop treatment) and to plan the re-institution of chronic therapy. They are also of use in the diagnosis of brain death, in assessing the suitability of potential organ donors and for medico-legal or forensic reasons. In addition to supportive investigations which are widely available (e.g. urea and electrolytes, glucose, calcium, magnesium, creatine kinase, liver function tests, clotting studies, anion gap, osmolality, blood gas analysis), specialist assays should be available at hospitals admitting acutely poisoned patients. These specific assays may be divided into two groups. Group 1 should be available on a 24 hour basis in all hospitals that admit patients with acute poisoning (Table 1). Group 2 includes those assays that are important in patient management but which are infrequently needed (Table 1). For these, arrangements need to be in place so that the assays can be obtained from specialist laboratories if they are not available on site. This may involve an arrangement with a supra-regional specialist toxicology laboratory or a subregional centre. It is the responsibility of each individual hospital to ensure that appropriate arrangements are in place and that staff can follow these arrangements when the need arises, including outside normal working hours. Laboratory staff should have contact details readily available for specialist laboratories providing these assays, together with information on how samples should be collected and transported. Clinical staff should discuss the use of group two assays with a local clinical biochemist and consider seeking advice from a Poisons Information Centre. In a national survey of major hospitals in the United Kingdom, most Group 1 assays were available

**Table 1.** Availability of assays.

Group 1 <sup>§</sup> : assays that should be available on a 24-h basis in all acute hospitals	
Carboxyhaemoglobin	Paracetamol
Digoxin	Paraquat (qualitative urine test)
Ethanol	Salicylate
Iron	Theophylline
Lithium	Valproate
Methaemoglobin	
Group 2: specialist or infrequent assays	
Arsenic	Methotrexate
Carbamazepine	Paraquat (quantitative plasma assay)
Cholinesterase	Phenobarbital
Ethylene glycol	Phenytoin
Lead	Thallium
Mercury	Thyroxine
Methanol	Toxicology screen

<sup>§</sup>Results for Group 1 assays should normally be available within a maximum of 2 hours (or sooner if possible) unless otherwise stated.

at all times. However, this was not the case for Group 2 assays. In this group assays for pharmaceuticals were more readily available than other assays: in particular, the availability of assays for cholinesterase, cyanide and heavy metals was poor. It is essential to be aware of the type of sample required and the units in which results are specified. A consensus meeting held by the Association for Clinical Biochemists agreed that concentrations for drugs should be reported in mass units per litre with the exception of iron, lithium, methotrexate and thyroxine. To avoid confusion it is recommended that, with the exception of these four agents, laboratories that report in molar units should also provide the result in mass units and should be encouraged for patient safety reasons to adopt the recommended use of mass units. **Reference:** 1. National Poisons Information Service; Association of Clinical Biochemists. Laboratory analyses for poisoned patients: joint position paper. *Ann Clin Biochem* 2002; 39:328–39.

### 4. Identifying the Patient at Risk – When to Rapidly Transfer to the Intensive Care Unit?

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**Background:** Poisonings represent one of the first causes of admission to the emergency room. Due to the significant morbidities and mortality that may result from overdoses, transfer to the intensive care unit (ICU) should sometimes be mandatory. Our objective was to identify clinical criteria indicating ICU transfer. **Methods:** Review of published data on severity criteria of poisoning and analysis of their pertinence in helping physicians in the emergency room (ER) to identify patients at risk requiring ICU transfer. **Results:** Poisoning should be considered as severe and transferred to the ICU if: (i) close monitoring is required in relation to a significant drug exposure; (ii) life-threatening symptoms occur including loss of consciousness, respiratory, and circulatory failure; (iii) the patient appears more vulnerable to the drug e.g. if presenting specific morbidities or chronic organ insufficiencies.<sup>1</sup> Poisoning features could result either from the direct effects of the drug or from non-specific complications (like aspiration pneumonia with a psychotropic drug or anoxic encephalopathy with cardiotoxicant-induced severe collapse). Absence of severe symptoms on hospital admission

does not necessarily mean no severe poisoning. Thus, assessing poisoning severity should not only rely on the routine criteria of severity and organ failure used in critical medicine but also include prognosticators, mainly in the case of exposure to substances resulting in organ injuries. Risk evaluation should take into account the dose, the formulation (sustained release), the different co-ingestions (additive or synergic effects), the delay in management since exposure, patient's medical conditions, the possible active metabolites from the ingested toxicant, and the possible occurrence of delayed symptoms. General scores (either physiological scores like APACHE-I or II, SAPS-II or III, and SOFA scores as well as specific poisoning scores like Poisoning Severity Score or Toxscore) are interesting for retrospectively stratifying poisoned patients amongst a study population but are quite limited for deciding at the individual level for patient referral to the ICU. Regarding psychotropic drugs, there is no clear relationship between the patient's Glasgow coma scale (GCS) score on admission and his final prognosis. Decreased GCS score does not mandate tracheal intubation in the emergency department.<sup>2</sup> The alert/verbal/painful/unresponsive (AVPU) responsiveness scale provides a rapid simple method of assessing consciousness level in most poisoned patients except those intoxicated with alcohol.<sup>3</sup> In cardiotoxicant overdose, occurrence of hypotension does not necessarily mean the presence of circulatory failure and does not necessarily require catecholamine administration. In contrast, in poisoned patients with a past history of significant hypertension or advanced cardiac disease, apparently normal values of blood pressure may be associated with progressive deterioration of microcirculation that would either not be identified, or recognized too late in the emergency department. Thus, abnormal signs of microcirculation resulting from hypotension should be assessed by regular monitoring in the ICU, including low urine output, increased concentrations of plasma lactate, serum creatinine and transaminases. We believe that any symptomatic patient in relation to cardiotoxicant ingestion should therefore be transferred to the ICU.<sup>1</sup> Prognosticators, including clinical, biological, ECG, and analytical parameters are drug-specific. They are generally more often identified based on retrospective approaches then prospectively assessed, ideally using multicentre studies, if their specificity, sensitivity, and predictive values appear interesting. Several prognosticators have been determined regarding antidepressants, acetaminophen, aspirin, chloroquine, colchicine, paraquat, corrosives and organophosphates. They may be helpful in indicating ICU transfer. Some of them are immediately available as soon as the patient is admitted to the ER. Others, based on specific assays (like verapamil concentrations in verapamil poisonings<sup>4</sup>) or complicated calculations (measurement of the terminal 40-millisecond frontal plane axis in tricyclic antidepressant poisoning<sup>5</sup>), appear less useful as they are not available in the majority of hospitals. Recently, in a case-control study, Manini and colleagues reported the utility of serum lactate concentration in the emergency room for predicting drug overdose fatalities, identifying the optimal cutoff point to be 3.0 mmol/L with 84% sensitivity and 75% specificity.<sup>6</sup> However, we assessed that the usefulness of serum lactate in predicting beta-blocker-overdose fatality appears limited, due to mild elevations despite extreme severity<sup>7</sup>, highlighting the impossibility of evaluating poisoning prognosis based on a unique measurement in the emergency room. On the other hand, excessive admission in the ICU may also result in non-useful expenses and limited bed availability. The patient's low risk was assessed when none of the following criteria was present in the emergency room<sup>8</sup>: need for intubation, seizures, unresponsiveness

to verbal stimuli,  $\text{PaO}_2 \geq 45$  mmHg, any rhythm except sinus, second- or third-degree atrioventricular block,  $\text{QRS} \geq 0.12$  s or systolic pressure  $< 100$  mmHg. In this study, of 151 low-risk patients, none developed a high-risk condition after admission, and none required an intensive care intervention. The use of these predictive criteria eliminated over half the intensive care days without compromising quality of care. **Conclusion:** ICU transfer may be mandatory if poisoned patients present with organ failure in order to set up adequate monitoring and invasive symptomatic treatments if necessary. Routinely available emergent prognosticators are required: they are drug-dependent. In contrast, general scores have limited interests at the individual level. **References:** 1. Mégarbane B, Donetti L, Blanc T, et al. [Treatment of acute poisoning by illicit drugs. Recommendations of the French Language Resuscitation Society (SRLF)]. [Article in French]. *Rev Prat* 2008; 58:871–81. 2. Ducan R, Thakore S. Decreased Glasgow Coma Scale score does not mandate endotracheal intubation in the emergency department. *J Emerg Med* 2009; 37:451–5. 3. Kelly CA, Upex A, Bateman DN. Comparison of consciousness level assessment in the poisoned patient using the alert/verbal/painful/unresponsive scale and the Glasgow Coma Scale. *Ann Emerg Med* 2004; 44:108–13. 4. Mégarbane B, Karyo S, Abidi K, et al. Predictors of mortality in verapamil overdose: usefulness of serum verapamil concentrations. *Basic Clin Pharmacol Toxicol* 2011; 108:385–9. 5. Sanaei-Zadeh H, Zamani N, Shahmohammadi F. Methods for the measurement of the terminal 40-millisecond (T40-ms) frontal plane axis in tricyclic antidepressant poisoning. *Resuscitation* 2011; 82:1255–6. 6. Manini AF, Kumar A, Olsen D, et al. Utility of serum lactate to predict drug-overdose fatality. *Clin Toxicol (Phila)* 2010; 48:730–6. 7. Mégarbane B, Deye N, Malissin I, et al. Usefulness of the serum lactate concentration for predicting mortality in acute beta-blocker poisoning. *Clin Toxicol (Phila)* 2010; 48:974–8. 8. Brett AS, Rothschild N, Gray R, et al. Predicting the clinical course in intentional drug overdose. Implications for use of the intensive care unit. *Arch Intern Med* 1987; 147:133–7.

##### 5. Acute Medical Effects of Radionuclides and Radiation: An Overview

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**Objective:** A wide spectrum of potential radiation exposure scenarios can result in different types of radiation exposure. External exposure, for instance, from a sealed radiation source, or internal exposure due to the intake of radionuclides, can occur. In the case of a nuclear disaster scenario there is also a possibility of a combination of external and internal radiation exposure. Depending on different types of radiation exposure scenarios the consequences in terms of diagnosing radiation-induced health damage, determining the cause, dealing with contamination/incorporation and pathophysiological and therapeutic principles will be different. The objectives are to address the basic differences between external and internal radiation exposure scenarios; to present in detail the acute radiation effects and the development of acute radiation syndrome as well as the most important aspects of radiation induced multi-organ involvement and multi-organ failure; and to discuss established therapeutic principles as well as new approaches in the therapy of radiation induced health impairments. **Methods:** The available literature regarding radiation effects and diagnostic and therapeutic strategies has been reviewed. **Results:**

Biological effects of ionizing radiation will start on the cellular level by energy absorption. Different physical effects, such as the Compton process and the photoelectric process for x- or gamma-rays will take place in this process. Damage on the molecular level could affect DNA-molecules as the most important targets resulting in base damage, single-strand breaks or even double-strand breaks. Double-strand breaks are considered the most serious DNA-lesions. The increasing occurrence of DNA-lesions and, especially, of double-strand breaks will lead to a higher risk of cell death.<sup>1</sup> From a pathophysiological point of view deterministic radiation effects can be differentiated from stochastic radiation effects. Deterministic radiation effects include acute radiation effects such as the hematopoietic syndrome. Deterministic radiation effects occur after a threshold radiation dose is exceeded and the severity will increase with increasing radiation exposure. The best known stochastic effect is the development of malignant tumors. The probability of their appearance will increase with an increasing absorbed radiation dose. Acute radiation syndrome will start with the so-called prodromal phase. Symptoms during the prodromal phase include: anorexia, nausea, vomiting, diarrhoea, fluid loss, fever, hypotension, headache and early erythema.<sup>1</sup> Depending on the absorbed radiation dose, after a latent period the manifestation takes place in different organ systems as syndromes of the hematopoietic system, the gastrointestinal system, the skin and the neurovascular system. Since the hematopoietic system is the most radio sensitive, the hematopoietic syndrome will occur at a lower dose than the other organ syndromes. Since in the case of a homogenous whole body radiation exposure all differentiated cells and stem cell pools of the organism will be affected, radiation induced multi-organ involvement, systemic inflammatory response syndrome and even multi-organ failure have to be considered in the clinical management of radiation accident victims.<sup>2</sup> External contamination with radionuclides has to be detected as soon as possible to carry out decontamination measures. In the case of intake or incorporation of radionuclides, the identification of the radionuclide must be the first step to be able to carry out a specific de-corporation therapy to reduce the resulting radiation dose. Combined radiation injuries will result from the combination of conventional trauma like wounds and burns with significant radiation exposure. The prognosis of patients with combined radiation injuries will be worse than from radiation exposure or conventional trauma alone. Therapeutic measures dealing with the hematopoietic system are most important. They include general measures like barrier nursing conditions, sufficient and immediate therapy of infections, or even prophylactic administration of antibiotic, antimycotic and antiviral substances. Specific therapeutic principles include the replacement with blood products, the administration of cytokines like G-CSF and GM-CSF, and the transplantation of hematopoietic stem cells.<sup>3–5</sup> Regarding radiation-induced multi-organ involvement, systemic inflammatory response syndrome and even multi-organ failure, therapeutic efforts are to be taken to stabilize the homeostasis and to reconstitute the function of organs and organ systems.<sup>2</sup> **Conclusion:** Radiation effects will occur at the molecular level, where DNA-molecules can be affected as the most important targets resulting in base damage, single-strand breaks or even double-strand breaks. Acute radiation effects can occur in different organ systems depending on the nature and the extent of radiation exposure. The development of radiation induced multi-organ involvement, systemic inflammatory response syndrome and even multi-organ failure have always to be considered in the clinical management of radiation accident victims. Hematopoietic

syndrome will more likely result from lower radiation exposure than the other organ syndromes, since the hematopoietic system is most vulnerable to ionizing radiation. Therefore diagnostic and therapeutic measures regarding the hematopoietic syndrome are of great importance in the clinical management of radiation exposed patients. Therapeutic measures include general measures and specific therapeutic measures like replacement with blood products, administration of cytokines, and transplantation of hematopoietic stem cells. Since radiation-induced multi-organ involvement or multi-organ failure will be associated with a poor prognosis in the patient, new therapeutic strategies to prevent the development of multi-organ failure in an early stage should be the focus in further research. **References:** 1. Hall EJ, Giaccia AJ. *Radiobiology for the Radiologist*. 7th ed. Philadelphia, USA: Lippincott Williams & Wilkins, 2011. 2. Meineke V, Fliedner TM. Radiation-induced multi-organ involvement and failure: challenges for radiation accident medical management and future research. *BJR Suppl* 2005; 27:196–200. 3. Dainiak N. Rationale and recommendations for treatment of radiation injury with cytokines. *Health Phys* 2010; 98:838–42. 4. Dainiak N, Ricks RC. The evolving role of haematopoietic cell transplantation in radiation injury: potentials and limitations. *BJR Suppl* 2005; 27:169–74. 5. Fliedner TM, Graessle D, Meineke V, et al. Pathophysiological principles underlying the blood cell concentration responses used to assess the severity of effect after accidental whole-body radiation exposure: an essential basis for an evidence-based clinical triage. *Exp Hematol* 2007; 35:8–16.

##### 6. Consequences of the Fukushima Disaster upon a European Country

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**Objective:** The earthquake and subsequent tsunami in Japan on March 11th, 2011 resulted in problems with the Fukushima nuclear power plant (NPP) and release of radioactive material in the environment. This disaster not only had enormous consequences for Japan but also affected countries worldwide. Shortly after the disaster the Dutch structure for nuclear incidents, the Unit Planning and Advice nuclear (EPAN) was activated. In the EPAN the Dutch Poisons Information Center advises on the medical aspects of exposure to ionising radiation and radioactive material. The activities undertaken in the Netherlands are presented as an example of the consequences for a country more than 12,500 km away from the original incident. Key issues to address: The first concern of the EPAN was to advise on a strategy for adequate protection of all Dutch citizens present in Japan at the time of the incident. These were personnel of the Embassy, travellers and people working for companies in Japan. Also the Dutch government wanted to compare the response of the Japanese government to the Dutch policy. Furthermore, advice was needed on the screening (and if necessary decontamination) of returning Dutch citizens and imported food and goods. Since the incident attracted a lot of media attention, there were many questions from press and public to be answered. **Problems:** In the aftermath of the Fukushima incident it proved to be very difficult to get reliable information on the radiological situation in the Fukushima area.

In the first weeks the situation at the NPP remained unstable and to predict radiation dose due to exposure to the released radionuclides was not easy. Monitoring of food from Japan was intensified in the Netherlands. Later, containers with goods coming from Japan were also screened for radioactive contamination. It appeared difficult to issue uniform advice in all European countries, as the intervention levels for countermeasures and decontamination differ among European countries. To overcome this problem conference calls with representatives of many European countries were carried out by the Health Security Committee of the European Commission in cooperation with WHO, to collect information on actions undertaken in different countries. These actions concerned travel advice, iodine prophylaxis and entry screening of aeroplanes, passengers and luggage coming from Japan. In the Netherlands, EPAn prepared information on iodine prophylaxis, sent iodine tablets to Japan for the Dutch citizens and set up a helpdesk for returning visitors. The EPAn remained activated until June 2011. **Conclusion:** An incident with a nuclear power plant has substantial consequences not only for the country directly involved, but also for many other countries worldwide. This means a lot of work and time investment for all persons concerned with incidents with ionising radiation. After the Fukushima disaster, it appeared that though all European countries were confronted with the same issues, their responses were different. This is due to different strategies and countermeasures, and confusing for the people involved. To solve this problem harmonisation of intervention levels in Europe is of utmost importance to be able to provide consistent advice in different EU countries.

### 7. The Role of the Norwegian Competence Centre for NBC Medicine during the Non-CBRN Terrorist Attacks in Norway on 22 July 2011

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**Objective:** To describe the involvement and usefulness of a pre-established centre for addressing chemical, biological, radiological, and nuclear (CBRN)-questions during a terrorist attack, even when it turned out to be a non-CBRN event. **Methods:** Summarize inquiries to the centre and the experiences of the centre staff during and after the attacks. **Results:** The attacks consisted of a bomb blast outside the government buildings at 3:25 pm (killing eight and wounding 30), and from 17:22 pm a shooting massacre at a youth political camp on a lake island (killing 68, wounding 58). The initial report from the paramedic at the bomb blast was "a toxic smell", and fear of it being a "dirty bomb" was communicated to the NBC-centre (nuclear, biological, and chemical). The NBC-centre involvement immediately after the blast consisted of establishing awareness among the triage teams for possible additional toxicological symptoms among the wounded. According to the centre routine, the NBC physician on call took part in and observed the hospital triage, but found no signs of toxic exposure. The hospital physicist on call surface-scanned the first five patients for radiation, with no findings. After the later shooting massacre, no signs indicated CBRN agents. However, the gunman had published a manifesto on the Internet, stating that he would fill bullets with nicotine to enhance damage. Rumours spread among health care professionals concerning possible toxic or radioactive compounds. The NBC centre received inquiries from the health authorities to investigate possible consequences.

The conclusion, after theoretical considerations, discussion with international colleagues, and clinical evaluation was that toxic impact was unlikely. Nevertheless, blood and urine samples were stored for later analyses, projectiles taken out of patients were scanned for radiation, and an official press release was prepared stating there were no signs of toxicity, mitigating rumours. Later ammunition analyses by the police revealed no nicotine or other toxic compounds. **Conclusion:** An established routine for immediate response in a terrorist event to confirm or disprove a CBRN threat is important to avoid treatment delay and spread of rumours. The function of a clinically oriented NBC centre as an addressee for CBRN questions may help decision-makers in a large-scale situation.

### 8. Pharmacokinetics and Outcomes in Massive Paracetamol Overdose

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**Objective:** There is a known association between increasing half-life and hepatotoxicity in paracetamol overdose.<sup>1</sup> We aimed to investigate the pharmacokinetics of massive paracetamol overdose to explore this association as well as the outcomes in these patients. **Methods:** Paracetamol overdoses were reviewed from two clinical toxicology units and overdoses of  $\geq 50$  g paracetamol were included. Data were extracted from a clinical database or from the medical record, including demographics, dose and time of ingestion, serial paracetamol concentrations and alanine transaminase (ALT), and N-acetylcysteine administration. The paracetamol concentration-versus-time data were analysed by a population approach using Monolix<sup>TM</sup>. One and two compartment open models with linear, non-linear and parallel elimination kinetics were tried. **Results:** There were 51 massive paracetamol overdoses with a median age of 32 years (Interquartile range [IQR]: 22–42 y; Range: 15–87 y) and 27 (53%) were female. The median ingested dose was 55 g (IQR: 50–70 g; Range: 48–200 g). The paracetamol concentration-versus-time data was best described with a one compartment model with first-order input and first order elimination. The population mean estimates of elimination rate constant (K), volume of distribution (Vd) and absorption rate constant (Ka) were 0.232 hr<sup>-1</sup>, 14.9 L and 0.90 hr<sup>-1</sup> respectively. Fourteen patients had an abnormal ALT. The median half-life for individual patients who developed abnormal ALT was 4.2 hr (IQR: 2.5–7.9 hr) which was significantly longer than for patients with normal ALT of 2.1 hr (IQR: 1.5–3.2 hr; p = 0.005). There was no association between dose and half-life, and no evidence of non-linear elimination. Five of the 14 patients with an abnormal ALT had NAC commenced within 8 hours. **Conclusion:** There was an increased apparent half-life in patients who developed an abnormal ALT, which was not explained by a larger ingested dose or non-linear elimination. The half-life in patients with a normal ALT was similar to that seen in patients taking paracetamol therapeutically with first-order elimination. A proportion of patients ingesting > 50 g paracetamol developed abnormal ALT despite early NAC treatment. **Reference:** 1. Prescott LF, Roscoe P, Wright N, Brown SS. Plasma-paracetamol half-life and hepatic necrosis in patients with paracetamol overdosage. *Lancet* 1971; 1:519–22.

### 9. The Effect of Ethanol on Paracetamol Absorption and Activated Charcoal Efficacy, in a Simulated Human Paracetamol Overdose

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**Objective:** This study evaluated whether ethanol in two different strengths affected the gastric emptying time, and if activated charcoal (AC) efficacy was altered in the presence of ethanol, in humans. Previous data on the ethanol influence are conflicting.<sup>1</sup> **Methods:** The study was an open, crossover, randomised human simulated overdose study, including 20 healthy male volunteers. Paracetamol (50 mg/kg) was used as marker drug. Interventions varied in ethanol strength in an ingested liquid: Day A 1068 mL water; Day B and C 60 g ethanol (1068 mL beer 7.2% v/v); Day D 60 g ethanol (187 mL vodka 37.5% v/v in 150 mL fruit juice). The liquid ingestions were distributed over 45 minutes and followed by paracetamol. AC (50 g) was dosed on Day C and D at 1-hour after the drug ingestion. Pharmacokinetic parameters (AUC[t(0)-t(last time point)], Tmax and Cmax) for the marker paracetamol, were calculated from serum-paracetamol concentrations collected at 12 time points. **Results:** Pharmacokinetic parameters for paracetamol are presented in the Table 1. **Conclusion:** Beer reduced the par-

**Table 1.** Pharmacokinetic parameters for paracetamol. Data are presented as mean [SD].

Study day	AUC (min*mg/L)	Tmax (min)	Cmax (mg/L)
A	9197 [1752]	53 [42]	50 [18]
B	10202 [2506]	105 [72]	46 [11]
C	6949 [2375]	59 [14]	41 [13]
D	8375 [2749]	39 [18]	51 [18]

acetamol absorption rate compared to water and stronger alcohol (p < 0.05), and the reduced rate might cause a longer drug-AC contact time. AC interrupts the paracetamol absorption and reduces the total amount of absorbed drug, regardless of the gastric ethanol concentration (p < 0.05). The study results do not challenge the present AC dose recommendations in paracetamol-ethanol co-poisonings. **Reference:** 1. Hoegberg LC, Angelo HR, Christophersen AB, et al. Effect of ethanol and pH on the adsorption of paracetamol to high surface activated charcoal, in vitro studies. *J Toxicol Clin Toxicol* 2002; 40:59–67.

### 10. Long Live the King! Comparing Prognostic Markers in Acetaminophen Poisoning Fatalities

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**Objective:** Identification of patients at risk of death after acetaminophen (APAP) poisoning remains challenging.

**Table 1.** The sensitivities and times to fulfillment of prognostic indicators in acetaminophen poisoning.

Prognostic indicator	Number of patients with sufficient data	Sensitivity, % (95% CI)	Median time from ingestion to criterion fulfillment, hours [IQR]	Median time from hospital admission to criterion fulfillment, hours [IQR]
KCC	68	80.3 (68.2,89.4)	90.8 [109.7]	17.8 [25.3]
MELD > 33	59	47.1 (33.3,61.3)	88.3 [66.7]	14.8 [18.5]
Lactate > 3.5 mmol/L	55	65.3 (50.4,78.3)	108.3 [98.3]	28.8 [15.8]
Phosphate > 1.2 mmol/L	31	79.3 (60.3,92.0)	112.4 [123.3]	17.6 [17.8]
KCC OR phosphate > 1.2 mmol/L	68	83.6 (71.9,91.9)	90.9 [103.6]	16.3 [10.6]
KCC OR lactate > 3.5 mmol/L	68	90.2 (79.8,96.3)	69.8 [97.8]	16.3 [12.4]

Each of the currently available prognostic indicators suffers from imperfect sensitivity. Moreover, how soon each indicator becomes positive is not well described. We sought to compare different prognostic markers in a large national cohort of patients whose in-hospital death was attributed to APAP poisoning. **Methods:** We performed a structured medical record review of patients hospitalized for APAP poisoning at one of 34 hospitals in eight Canadian cities from 1980–2010. We identified all in-hospital deaths meeting the following criteria: acute or chronic overdose with known time of ingestion, coagulopathy (peak INR > 1.5 or PT > 16 seconds), and encephalopathy grade > or = 1. We calculated the sensitivity of each prognostic indicator in those patients with sufficient laboratory data. The time interval from either ingestion or hospital presentation until each prognostic indicator was met was also calculated. The King's College Criteria (KCC) were defined as serum pH < 7.3 or all of PT > 100 seconds (INR > 6.5), creatinine > 300  $\mu$ mol/L and grade 3 or 4 encephalopathy. **Results:** Of 173 fatalities, 68 met our inclusion criteria. The sensitivities and times to fulfillment of each prognostic indicator are shown in Table 1. **Conclusion:** In this cohort of Canadian fatalities due to acetaminophen poisoning, combining the King's College Criteria with a lactate over 3.5 mmol/L provided the highest sensitivity and the shortest time interval from ingestion to criteria fulfillment. In most patients who died, the prognostic criteria became positive during the first day of hospitalization.

### 11. The Predictive Value of Serum Alanine Transaminase Activity on First Presentation to Hospital in Patients with Paracetamol Poisoning

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**Objective:** At present the only treatment strategy for paracetamol (acetaminophen) poisoning is replenishment of cellular glutathione with antidotes such as acetylcysteine. For successful translation from rodent models into humans, new therapies need to be tested in trials that specifically recruit patients with a high risk of liver injury at first presentation to hospital, a time when liver cell death may be preventable. The objective of this study was to test serum alanine transaminase (ALT) activity at hospital admission as a predictor of subsequent paracetamol-induced liver injury. **Methods:** Patients admitted to the Royal Infirmary of Edinburgh, UK with excess paracetamol ingestion that required treatment with acetylcysteine were included in this

study. The study started from March 2011 and is ongoing. Patients who did not complete antidote treatment were excluded. The performance of the admission ALT activity (less than or greater than the upper limit of our hospital's normal range) was tested as a predictor of: endpoint 1 - doubling of ALT from admission to end of initial acetylcysteine therapy and endpoint 2 - peak ALT > 1000 u/L. **Results:** A total of 131 patients have been studied up to November 2011 (male:female numbers: 48:83, mean age: 36 yrs, standard deviation: 14 yrs). Ninety-four patients presented to hospital within 8 hrs of drug ingestion, 10 presented 8–24 hrs post-ingestion, 1 presented 24–36 hrs post-ingestion, 2 presented > 36 hrs post-ingestion and 24 were staggered ingestions. On admission to hospital, serum ALT activity was elevated above the upper limit of the normal range (> 50 u/L) in 24 patients. For endpoint 1 the positive predictive value (PPV) of admission ALT was 9.5% and the negative predictive value (NPV) was 97.3%. For endpoint 2 PPV of admission ALT was 16.7% and NPV was 100%. **Conclusion:** On first presentation to hospital serum ALT activity within the normal range is a predictor of no subsequent liver injury following completion of acetylcysteine therapy. However, an elevated admission serum ALT activity (> 50 u/L) is a poor predictor of progressive paracetamol-induced liver injury and, based on our data so far, would not be a useful marker to guide inclusion into therapeutic trial.

### 12. The Expert Witness in Clinical Toxicology

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**Objective:** To show from personal experience a scheme for considering forensic aspects of clinical toxicology. **Introduction:** The physician with an interest in clinical toxicology finds from time to time that his or her services are requested by lawyers, the police, or the coroner (medical examiner). These personal views are based on practice in England and Wales, but the general principles should be widely applicable. Experts, in order to help the court, have to answer a series of questions put by others – for example, did this dose of this drug kill this patient? **Methods:** First, physicians must decide whether the knowledge and experience they possess permit them to answer the questions asked. If there is any doubt, they should decline the case.<sup>1</sup> The stages in considering a case, having understood the questions, and what the standard of proof will be are as follows: 1. assemble the evidence from clinical history and witness statements; physical or post-mortem examination; and laboratory tests, and supplement or corroborate expert views with informa-

tion from textbooks and scientific papers; 2. analyze the evidence by considering the arguments for and against propositions. For this, DoTS (considerations of Dose-response, Time-course, and Susceptibility) can be helpful.<sup>2</sup> 3. present a balanced opinion as an answer to the questions. Dangers to be aware of are arguments that if B followed A, B was because of A; and that if A is a sufficient cause of B, it is the necessary cause of B: it is essential to consider alternative (competing) causes such as natural disease. The physician compiles a written report, and later presents views in court.<sup>3</sup> Since both the evidence and the cross-examination of a witness will be based on the report, it is very important to take care that it portrays one's views and is clear for a lay person to follow; that it is consistent both with logic and the facts; and that one's views in court are consistent with it. **Discussion:** Lawyers are paid to question what experts say, and may use flattery, aggression, charm and other weapons to lead experts away from views they honestly hold and wish to maintain. Awareness of the weapons lawyers use can help to protect against them. Clarity, honesty, and reiteration of one's views can help. **Conclusion:** The clinical toxicologist has to deploy his or her clinical experience and scientific understanding to provide satisfactory medicolegal advice. It is best to take a broad view that takes in alternative explanations for a given set of facts and weigh evidence for and against each explanation. Clarity, honesty, and reiteration of one's views can help. **References:** 1. General Medical Council. Supplementary Guidance - Acting as an expert witness. London 2008. Available at: [http://www.gmc-uk.org/guidance/ethical\\_guidance/expert\\_witness\\_guidance.asp](http://www.gmc-uk.org/guidance/ethical_guidance/expert_witness_guidance.asp) [accessed 31 Jan 2012]. 2. Aronson, JK, Ferner RE. Clarification and terminology in drug safety. *Drug Safety* 2005; 28:851–70. 3. Norman E. Legal Considerations. In: Ferner RE. *Forensic Pharmacology. Medicines, Mayhem and Malpractice*. Oxford, England: Oxford University Press, 1996.

### 13. Interpretation of Laboratory Drug Analyses for Forensic and Medicolegal Purposes

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**Objective:** Clinical toxicologists are sometimes asked to help the court with the interpretation of drug or chemical analyses as part of criminal or medicolegal proceedings. Scenarios include eliciting the role of drugs or other toxins in a death or in the behaviour of a suspect or victim, evaluation of criminal poisoning or adulteration, drug-facilitated sexual assault, non-accidental poisoning in children and driving under the influence. Adherence to drug treatment may sometimes be important in death (e.g. in epilepsy) and forensic analysis may also be relevant for legal proceedings relating to occupational exposure. This presentation will discuss the samples that may be available and common pitfalls in their interpretation. Further detailed information is available in several published reviews.<sup>1–3</sup> General principles: Analytical evidence should be considered in the context of all other evidence available, especially the clinical features of the exposed individual. The validity of data needs careful consideration<sup>4</sup>; this depends on chain of custody, appropriate sample collection and labelling, use of an appropriate anticoagulant/preservative and the accuracy and limits of detection of the analyses performed. Many clinical toxicologists are not familiar with all these issues and must restrict their comments to areas of expertise. Some analyses are only qualitative,

giving evidence of exposure only, while quantitative analysis may allow conclusions to be drawn about dose and toxicity. Particular care is needed to take account of the units used to report concentrations and whether these refer to the free acid/base or the salt form. Samples and interpretation: (a) Blood: Analyses are done on whole blood, serum or plasma and this may affect interpretation. For example chloroquine concentrations are substantially higher in whole blood than plasma. It may be possible to relate plasma concentrations to clinical effects, but there is substantial variability between individuals and tolerance and habituation need to be considered. The timing of blood sampling in relation to exposure and to the events under consideration by the court may be crucial. For substances with zero order elimination (e.g. ethanol) it is possible to back-extrapolate concentrations from the time of sampling to the time of interest using typical population elimination values, allowing estimation of blood alcohol concentration at the time of driving from a sample taken hours later. For substances with first order metabolism, including most drugs, such back-extrapolation is likely to be misleading because the exponential concentration-time relationship results in multiplication of inaccuracies. Further information about timing of drug administration may be inferred from concentration of metabolites in relation to parent drug, with a higher ratio suggesting a longer time since exposure. Interindividual variability, including pharmacogenetic factors, and the importance of incomplete distribution of samples taken soon after exposure (e.g. digoxin, lithium) also need consideration. For blood samples taken after death, interpretation is complicated by post mortem changes resulting from redistribution, putrefaction (producing for example ethanol, acetaldehyde or phenylethylamine), dehydration (e.g. from heat), dilution (e.g. in drowning), ongoing drug metabolism (e.g. cocaine) or synthesis (e.g. GHB). Post mortem redistribution is especially important, involving movement of drugs from the gut, liver, heart or lungs to central veins so that central blood samples (e.g. ventricular blood) often have higher concentrations than peripheral blood (e.g. femoral vein). The central to peripheral ratio varies with different drugs, further complicating interpretation and tends (with exceptions) to be higher for weak bases with large volumes of distribution. Redistribution also depends on time between death and sampling, body position and use of resuscitation. Post mortem blood samples are often employed to determine if a drug is the cause of death using tables of drug concentrations associated with fatality. The expert must be aware that the factors described above may have substantial effects on drug concentration and that there is substantial overlap between concentrations associated with death and survival. (b) Urine: This is comparatively simple to obtain and has some advantages over blood in that drugs or their metabolites may be concentrated in urine and may persist in urine after they have disappeared from the blood stream. However, urinary concentrations are less correlated with clinical effects. (c) Others: Drugs may be detected in stomach contents, although analysis is generally qualitative rather than quantitative. Pitfalls include non-homogeneous distribution of drugs in the stomach contents and diffusion from the blood back into the stomach post mortem. Vitreous humour (VH) analysis can be useful post mortem because drugs sequestered here are protected from putrefaction, charring, trauma and micro organisms. There is considerable published evidence of ethanol concentrations in VH but less for other substances, although these may persist in VH when blood concentrations are no longer detectable. Many drugs are

concentrated in bile and may also be detectable there when no longer found in blood. As a result of its rich blood supply drugs distribute to bone marrow, which may be available in advanced decomposition. There is, however, limited information available correlating bone marrow with blood concentrations of drugs in life or after death.<sup>5</sup> Analysis of homogenised tissue from organs such as liver, brain or muscle is sometimes of value; tissue from injection sites may contain high concentrations of an implicated drug. Longer term exposure to drugs and chemicals may be inferred from hair or nail analysis, but this is not considered further in this presentation. *Conclusion:* Expert interpretation of laboratory analyses can be very valuable, but an understanding of drug metabolism and kinetics in life and death is essential. All available evidence and potential interpretations should be taken into account to withstand detailed legal scrutiny and avoid misleading the court. *References:* 1. Flanagan RJ, Connally G. Interpretation of analytical toxicology results in life and at post-mortem. *Toxicol Rev* 2005; 24:51–62. 2. Ferner RE. Post-mortem clinical pharmacology. *Brit J Clin Pharmacol* 2008; 66:430–43. 3. Kennedy MC. Post-mortem drug concentrations. *Intern Med J* 2010; 40:183–7. 4. Dinis-Oliveira RJ, Carvalho F, Duarte JA, et al. Collection of biological samples in forensic toxicology. *Toxicol Mech Methods* 2010; 20:363–414. 5. Cartiser N, Bévalot F, Fanton L, et al. State-of-the-art of bone marrow analysis in forensic toxicology: a review. *Int J Legal Med* 2011; 125:181–98.

#### 14. Can Postmortem THC Blood Levels be used to Estimate Antemortem Impairment?

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*Objective:* Marijuana is second only to alcohol as the most widely abused substance worldwide, and the number one drug found in driving under the influence of drugs (DUID) cases. The plasma levels of the active component of cannabis, D-9-tetrahydrocannabinol (THC), correlate with impairment: plasma THC > 2–5 ng/mL established impairment; THC levels above 5–10 ng/mL indicated severe impairment<sup>1</sup>; drivers with THC > 5 ng/mL are 6.6 times more likely to be killed in a traffic accident than those without THC; drivers with THC > 3 ng/mL were at increased risk of being judged impaired<sup>2</sup>. *Methods:* Many European countries have DUID levels for THC of ≤ 2.0 ng/mL in plasma<sup>3</sup>, and 17 states in the USA have zero tolerance laws for THC. Until recently, no information was available regarding the post-mortem redistribution (PMR) of THC, or whether forensic whole blood samples from MVA fatalities could be used for assessment of antemortem impairment. *Results:* The first demonstration of PMR of THC (2011), found that THC undergoes only modest PMR: average heart-to-iliac blood ratio 1.5 (range: 0.3–3.1). *Conclusion:* Since the blood:plasma ratio for THC is approximately 0.5:1<sup>4</sup>, and the whole blood heart-to-iliac ratio averages less than 2:1, the author proposes that peripheral post-mortem whole blood THC levels can be utilized for assessing antemortem impairment, using the known published plasma impairing levels. *References:* 1. Papafotiou K, Carter JD, Stough C. The relationship between performance on the standardised field sobriety tests, driving performance and the level of Delta9-tetrahydrocannabinol (THC) in blood. *Forensic Sci Int* 2005; 155:172–8. 2. Ramaekers JG, Moeller MR, van Ruitenbeek P, et al. Cognition and motor control as a function of Delta(9)-THC concentration in serum and oral fluid: Limits of impairment. *Drug*

*Alcohol Depend* 2006; 85:114–22. 3. Jones AW, Holmgren A, Kugelberg FC. Driving under the influence of cannabis: a 10-year study of age and gender differences in the concentrations of tetrahydrocannabinol in blood. *Addiction* 2008; 103:452–61. 4. Giroud C, Menetrey A, Augsburger M, et al. Delta(9)-THC, 11-OH-delta(9)-THC and delta(9)-THCCOOH plasma or serum to whole blood concentrations distribution ratios in blood samples taken from living and dead people. *Forensic Sci Int* 2001; 123:159–64.

#### 15. A Randomised Controlled Trial of High-Dose Immunosuppression in Paraquat Poisoning

Gawarammana I<sup>1,2,3</sup>, Buckley NA<sup>2,16</sup>, Mohammed F<sup>2</sup>, Naser K<sup>4</sup>, Jeganathan K<sup>5,6</sup>, Munasinghe A<sup>7</sup>, Ariyananda PL<sup>8</sup>, Wannapak K<sup>9,10</sup>, Tomenson J<sup>11</sup>, Wilks M<sup>12</sup>, Eddleston M<sup>13,14</sup>, Dawson AH<sup>2,15</sup>.  
<sup>1</sup>Department of Medicine; <sup>2</sup>South Asian Clinical Toxicology Research Collaboration, Faculty of Medicine, University of Peradeniya, Sri Lanka; <sup>3</sup>Australian National University, Canberra, Australia; <sup>4</sup>Peradeniya Hospital; <sup>5</sup>Anuradhapura Hospital; <sup>6</sup>Rathnapura Hospital; <sup>7</sup>Matara Hospital; <sup>8</sup>Faculty of Medicine, University of Ruhuna, Sri Lanka; <sup>9</sup>Therapeutics Research Centre, School of Medicine, University of Queensland, Brisbane, QLD, Australia; <sup>10</sup>Department of Forensic Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; <sup>11</sup>Causation Ltd, UK; <sup>12</sup>Swiss Centre for Applied Human Toxicology, University of Basel, Switzerland; <sup>13</sup>Scottish Poisons Information Bureau, Royal Infirmary of Edinburgh; <sup>14</sup>Clinical Pharmacology Unit, University of Edinburgh, UK; <sup>15</sup>Clinical School, Royal Prince Alfred Hospital; <sup>16</sup>Professorial Unit, Department of Medicine, University of New South Wales, Sydney, Australia

*Objective:* Intentional self-poisoning with paraquat herbicides is a major problem in rural Asia, and the Pacific. Paraquat self poisoning has the highest recorded case fatality (~70%) for a pesticide. There is no proven antidote, however, immunosuppression with cyclophosphamide, methylprednisolone and dexamethasone has widely become the treatment of choice in many parts of the world. However, evidence of clinical benefit is weak. We aimed to determine whether the addition of immunosuppression to supportive care offers benefit in resource poor Asian district hospitals. *Methods:* We compared immunosuppression (cyclophosphamide up to 1 g/day for two days, methylprednisolone 1 g/day for 3 days and dexamethasone 8 mg three times a day for 14 days) with saline and placebo tablets in a double-blind randomised placebo-controlled trial. Mortality at 3 months was the primary outcome. *Results:* The trial was stopped early as paraquat was banned in Sri Lanka. At this time, there were 605 patients with a history of paraquat ingestion. There were 407 who met inclusion criteria. Two hundred and ninety-eight patients consented and were randomised to receive immunosuppression or saline and placebo. Overall mortality in the trial was 208/298 (69.8%). There was no difference in case fatality between patients in placebo group (108/152 [71.05%]) and immunosuppression group (100/146 [68.4%]). (Difference between fractions 2.5%, 95% CI: -7 – 12). There was also no difference in median time to death between the placebo group and the immunosuppression group (2 days vs 1.92 days respectively). *Conclusion:* We found no evidence that this immunosuppression regimen improves survival in paraquat poisoned patients and thus this popular treatment should no longer be recommended.

### 16. The Utility of Extracorporeal Treatment for Acute Thallium Poisoning: The First Recommendation from the Extracorporeal Treatment in Poisoning Workgroup

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*EXTRIP, The Extracorporeal Treatments in Poisoning Workgroup*

**Objective:** Extracorporeal treatment (ECTR) is commonly used in poisoning despite a lack of controlled human trials demonstrating efficacy. The Extracorporeal Treatment in Poisoning (EXTRIP) workgroup is a collaboration of diverse international experts with the overarching goal of systematically studying the existing literature and developing uniform recommendations for ECTR in poisoning. We report the results of the first poison studied: thallium. **Methods:** Rigorous criteria were developed to identify all relevant publications. Data were extracted by a subgroup comprised of three EXTRIP participants. After comparison for consistency and adjudication of discrepancies, preliminary results were reviewed by the entire EXTRIP workgroup who voted on closed recommendation questions. Results were reviewed, discussed, and a final vote was taken to achieve consensus. **Results:** The literature search (last accessed on 10/24/2011) and hand-search yielded 76 articles, 45 with original patient data. Only case reports and case series were identified (no controlled trials or observational studies), yielding a quality of evidence for all recommendations of “very poor”, (D) according to GRADE. Data from 62 patients included 10 fatalities, all following massive ingestion or 48-hour delay to ECTR. Despite thallium’s low molecular weight and negligible protein binding, its clinical dialyzability is limited by its large volume of distribution. Nevertheless, ECTR provides superior hourly removal than renal or stool elimination via Prussian Blue. Although there is a lack of evidence with newer ECTR modalities, EXTRIP agreed that thallium is slightly dialyzable (low-moderate evidence) and recommended ECTR in SEVERE thallium poisoning (1D) if: Exposure is highly suspected based on history or clinical features (1D); or the serum thallium concentration is 0.4–1.0 mg/L (3D) or > 1.0 mg/L (1D). ECTR is preferentially initiated < 48 hours after exposure (1D), and should be continued until levels are < 0.1 mg/L for a minimum of 72 hours (2D). Finally, intermittent hemodialysis is recommended as the preferred initial ECTR (1D), and intermittent hemoperfusion or CRRT modalities are valid alternatives if intermittent hemodialysis is unavailable (1D). **Conclusion:** Despite thallium’s low clinical dialyzability, ECTR provides superior hourly removal than both renal or stool elimination via Prussian Blue, and the workgroup strongly recommended the use of ECTR in severe thallium poisoning.

### 17. The Evidence for Activated Charcoal in Resource Poor Settings: A Systematic Review

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**Objective:** Poisoning is unfortunately a common occurrence worldwide with relatively higher mortality in resource-poor settings (RPS), and oral activated charcoal (AC) is an inexpensive, widely available decontaminant with a favorable side effect profile. However, recent clinical trial results have called into question its benefit.<sup>1</sup> This systematic review was done to examine the recent clinical evidence evaluating standard AC

decontamination in international RPS. **Methods:** A systematic review of the recent (past 20 years) literature was conducted on both single dose activated charcoal (SDAC) and multi-dose activated charcoal (MDAC) looking for the clinical evidence that supports its use in RPS. RPS was defined as environments where routine antidotes are either unavailable or prohibitively expensive. EMEDLINE Pubmed, Cochrane Databases, Clinicaltrials.gov, and Google Scholar were searched for published studies in the English language in the last 20 years using the terms “activated charcoal” in addition to the following: poison, overdose, ingestion, activated charcoal, gastric decontamination, single dose activated charcoal, multi-dose activated charcoal, or multiple-dose activated charcoal. **Results:** Out of all eligible studies published, 64 total studies met criteria for inclusion. Of these, there were 4 MDAC trials (3 prospective, 1 retrospective) and 7 SDAC trials (5 prospective, 2 retrospective) with analyzable efficacy data. Of these, two studies showed mortality benefit, while most others were underpowered to show a benefit. Subgroup analysis suggested greatest benefit for organic phosphorous pesticides and cardiac glycosides. Pooling two large studies (5,440 patients total) that addressed adverse events with AC administration demonstrated excellent safety with 1.4% incidence of aspiration overall. **Conclusion:** This systematic review of the past two decades of literature evaluating the efficacy of AC in RPS found excellent support for SDAC in undifferentiated overdose presenting in RPS and demonstrated benefit of MDAC for selected poisonings, particularly organic phosphorous pesticides and cardiac glycosides in that order. In addition, AC administration was safe and AC aspiration appears to be extremely rare. **Reference:** 1. Jürgens G, Hoegberg LC, Graudal NA. The effect of activated charcoal on drug exposure in healthy volunteers: a meta-analysis. *Clin Pharmacol Ther* 2009; 85:501–5.

### 18. Beyond Standard Anticholinergics: The Use of Physostigmine for Reversal of Somnolence and Delirium in a Cohort of Overdose Patients

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**Objective:** Physostigmine was used frequently for reversal of anticholinergic toxicity until an article in 1980 by Pentel and Peterson described an association between its use and the development of asystole in two patients with severe cyclic antidepressant (CA) overdoses. Publication of these cases caused a paradigm shift as many clinicians began to broadly interpret risk in treating not only patients with CA toxicity but also in using physostigmine for non-CA depressant intoxications. There appears to be a resurgence of use of this antidote, however, as recent publications describe successful reversal of toxicity in overdoses involving drugs such as quetiapine, olanzapine and cyclobenzaprine. Our objectives are to describe types of overdoses treated as well as adverse effects and outcomes of patients treated with physostigmine on our Toxicology Consultation Service. **Methods:** Retrospective review (1/1/2011–11/15/2011) covering 10½ months of a bedside Toxicology Consultation Service. Initial review performed of ACMT Toxic case registry data for our site, a tertiary-care referral center in the Eastern US. Cases in which physostigmine was used were further reviewed for efficacy, adverse effects and other outcomes data. **Results:** Physostigmine was administered for 16 unique patients (16/482

consultations) a total of 20 times (including one drip administration). Indications for use included reversal of coma and CNS depression, reversal of central anticholinergic toxicity and reversal of bothersome peripheral anticholinergic effects. Overdoses included: antihistamines/anticholinergics (5 diphenhydramine, 1 promethazine, 1 hydroxyzine, 1 Donnato [phenobarbital, hyoscyamine, atropine and scopolamine]), atypical antipsychotics (3 quetiapine, 2 olanzapine, 1 aripiprazole) and 3 cyclobenzaprine. Reversal was effective in 14/16 with intubation avoided in 4 patients and severe delirium/agitation attenuated in 3. Others had mild-moderate delirium/hallucinations or anticholinergic peripheral effects attenuated. Vomiting occurred in two patients and one individual experienced a panic attack upon reversal from Donnato intoxication. No episodes of bradycardia or other arrhythmia occurred. Physostigmine was ineffective in reversing delirium in one ingestion involving olanzapine and incompletely reversed somnolence, dry mouth and urinary retention in another patient with quetiapine and lorazepam ingestion. **Conclusion:** Physostigmine was safe and useful in reversing toxicity from a variety of agents including antihistamines/anticholinergics, certain atypical antipsychotics and cyclobenzaprine.

### 19. Mechanisms of Envenoming: An Overview of their Relevance in Treating Patients

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**Objective:** To review pathophysiological mechanisms of envenoming by animals as a guide to improving clinical management. **Methods:** Literature review together with published and unpublished clinical observations. **Results:** Envenoming by animals is a natural experiment, unaffected by ethical constraints, during which venom toxins in various undetermined doses stimulate or block a variety of physiological receptors. The effects on the human patient, although of no evolutionary relevance to the venomous animal, may reveal physiological mechanisms of whose complications the clinician should be aware. In some cases, a venom effect (e.g. defibrinogenation, lowering of blood pressure, inhibition of platelet activity etc) may suggest a therapeutic application. Shock: Hypotension, with hypoperfusion and other consequences in human victims, including acute kidney injury, is an effect of many vertebrate and invertebrate toxins. Notable examples are the early, often transient, shock and syncope in people envenomed by vipers and Australasian elapid snakes, helodermid lizards, scorpions and cnidarians. In the case of Australian brown snakes (*Pseudonaja*) and tiger snakes (*Notechis*), this has been attributed to pulmonary thromboembolism, based on studies in dogs<sup>1</sup>, but humans patients lack the clinical features to be expected if this were the mechanism (breathlessness, bronchospasm, chest pain, haemoptysis etc.). A more plausible explanation is the action of “autocoids”, toxins that activate endogenous pharmacological cascades. These include oligopeptide ACE-inhibitors and BPPs and other kininogen activators. Shock occurring later after envenoming has several possible causes including hypovolaemia resulting from extravasation into the bitten limb and elsewhere, haemorrhage, vasodilatation and anaphylaxis, both primary, as a direct effect of venom toxins (e.g. Helodermid lizard envenoming)<sup>2</sup>, and resulting from IgE-mediated sensitisation to venom through previous exposure (e.g. after Hymenoptera stings and, less commonly, after snake bites). Severe envenoming by both Old World and New World scorpions may involve initial hypertension attributable to the “autonomic storm” of catecholamine

release followed by hypotension of myocardial origin.<sup>3</sup> Bleeding and clotting disturbances: Snake venom enzymes, in the hands of Oxford's Gwyn Macfarlane and others<sup>4</sup>, proved useful tools in the elucidation of physiological blood clotting cascades. However, life-threatening haemostatic disturbances also involve actions on platelets and the vascular endothelium (metalloproteinase haemorrhagins). Some of these activities have prompted ideas for new drugs.<sup>5</sup> Acute kidney injury (AKI): In envenoming by some snakes, spiders, scorpions, Lepidoptera and other animals, AKI may be a fatal or permanently debilitating complication. Many mechanisms have been identified including direct nephrotoxicity, secondary effects of profound shock, thrombotic microangiopathy, microangiopathic haemolytic anaemia<sup>6</sup> and "pigment nephropathy". These aetiologies suggest various different types of preventive and therapeutic intervention. Autonomic nervous system activation: The classic biphasic pattern of envenoming by *Leiurus*, *Androctonus*, *Tityus* and *Hotentota* species suggests release of parasympathetic followed by adrenergic mediators, creating an "autonomic storm"<sup>3</sup> and prompting treatment with vasodilators such as the  $\alpha$ -1 blocker prazosin. Some syndromes of snake bite envenoming, such as by mambas (*Dendroaspis*) and bushmasters (*Lachesis*), include intense salivation, gastrointestinal symptoms and hypotension, suggesting autonomic nervous system activation for which ancillary pharmacological treatment in addition to antivenom might be effective. Neuromuscular blockade: Envenoming by snakes whose venoms contain only post-synaptic toxins [e.g. cobras (*Naja*) and death adders (*Acanthopis*)] may respond within minutes to anticholinesterases (7) and within 1–2 h to specific antivenoms, while reversibility of toxin binding to the ACh receptor by antibodies has been demonstrated experimentally.<sup>8</sup> However, pre-synaptic toxins in venoms of kraits and most Australasian elapids destroy nerve endings so that reversal by these interventions seems impossible.<sup>9</sup> Unexplained symptoms: A characteristic presenting symptom of common krait (*Bungarus caeruleus*) envenoming in South Asia, is severe, crescendo abdominal pain. A mamba intestinal toxin (prokineticin) like venom component might explain this symptom. Excruciating pain radiating up the bitten limb has been described in patients envenomed by South American coral snakes (e.g. *Micrurus lemniscatus*) suggests a toxin acting directly on pain-conducting C-fibres.<sup>10</sup> **Conclusion:** As in other branches of toxicology, understanding pathophysiological mechanisms is essential for predicting and anticipating the course of envenoming following bites and stings by venomous animals. Appropriate ancillary pharmacological treatments may be tested for their ability to prevent or ameliorate the effects of envenoming. **References:** 1. Tibballs J. The cardiovascular, coagulation and haematological effects of tiger snake (*Notechis scutatus*) prothrombin activator and investigation of release of vasoactive substances. *Anaesth Intensive Care* 1998; 26:536–47. 2. Piacentini J, Curry SC, Ryan PJ. Life-threatening anaphylaxis following gila monster bite. *Ann Emerg Med* 1986; 15:959–61. 3. Trejo E, Borges A, Nañez B, et al. *Tityus zuluianus* venom induces massive catecholamine release from PC12 cells and in a mouse envenomation model. *Toxicol* 2012; 59:117–23. 4. Macfarlane RG. Russell's viper venom, 1934–64. *Br J Haematol* 1967; 13:437–51. 5. Clemetson KJ, Lu Q, Clemetson JM. Snake venom proteins affecting platelets and their applications to anti-thrombotic research. *Curr Pharm Des* 2007; 13:2887–92. 6. Schneemann M, Cathomas R, Laidlaw ST, et al. Life-threatening envenoming by the Saharan horned viper (*Cerastes cerastes*) causing micro-angiopathic haemolysis, coagulopathy

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## 20. Snake Bite First Aid: Interest of Experimental Studies

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**Objective:** Species specific antivenins are effective in reducing toxicity from bites by venomous snakes and are the only treatment necessary when readily available. In areas with good transportation systems, advanced emergency medicine services and rapid access to medical facilities that stock antivenins for the region, first-aid measures are generally not necessary and may be harmful. In parts of the world where medical services and antivenins are not available, or in situations with long transport times to a medical facility, first aid measures have been proposed to alter morbidity and mortality. The objective is to review experimental studies of the efficacy of first aid measures for snakebites. **Methods:** A systematic literature review was undertaken to identify first aid measures that have been proposed or used to treat poisonous snakebites. MedLine searches were performed using the search words snake bite and first aid. Review articles and toxicology textbooks were reviewed. **Results:** Measures that have been proposed as first aid measures include: tourniquets<sup>1</sup>, incision and suction<sup>1,2</sup>, extraction devices<sup>2</sup>, electric shock<sup>3</sup>, pressure-immobilization bandages<sup>4–8</sup>, pressure pads<sup>9</sup>, a localizing circumferential compression device<sup>10</sup>, and nitric oxide<sup>11</sup>. For subcutaneous injection of venom, venom reaches the systemic circulation via lymphatic flow. Measures which delay or arrest lymphatic flow while preserving arterial and venous flow sequester venom and delay systemic toxicity, though such a strategy can increase local toxicity. **Conclusion:** Though a number of first aid measures have been proposed to treat snakebites, few have withstood the test of scientific investigation. While tourniquets may prevent mortality, they do so at the sacrifice of the limb. Pressure-immobilization bandages, pressure pads, and localizing circumferential compression devices sequester venom at the site of the bite by inhibiting lymphatic flow and have utility with neurotoxic venoms with minimal local toxicity. When used with venoms with local toxicity, these techniques delay systemic absorption of venom but increase local tissue necrosis. The nitric oxide donor glyceryl trinitrate has recently been shown to inhibit lymphatic flow and delay the onset of respiratory arrest in a rat model of *Pseudonaja textilis* (Eastern Brown snake) toxicity. **References:** 1. Gold BS, Dart RC, Barish BA. Bites of venomous snakes. *N Engl J Med* 2002; 347:347–56. 2. Alberts MB,

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## 21. Clinical Effects and Antivenom Dosing in Brown Snake (*Pseudonaja spp.*) Envenoming - Australian Snakebite Project (ASP-14)

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**Objective:** Brown snake (genus *Pseudonaja*) is the most medically important group of snakes in Australia. There has been controversy over the dose of antivenom in brown snake envenoming with escalating doses over the last 20 years. We investigated the clinical and laboratory features of definite *Pseudonaja spp.* bites and antivenom treatment. **Methods:** Patients with definite brown snake bites were recruited as part of the Australian Snakebite Project (ASP) based on expert identification of the snake or detection of *Pseudonaja* venom in pre-antivenom blood samples. Demographics, clinical information, laboratory tests and antivenom treatment are recorded prospectively for ASP. **Results:** There were 138 definite brown snake (*Pseudonaja spp.*) bites [median age 42 y (2 to 81 y); 100 males] included in the study and systemic envenoming occurred in 122 (88%) of cases. There were 15 non-envenomed patients and one snake handler who had venom anaphylaxis. Envenoming was charac-

terised by venom induced consumption coagulopathy (VICC) in all cases, with complete VICC in 100 (82%) and partial VICC in 22 (18%). Systemic symptoms occurred in 57 patients (47%). Myotoxicity did not occur and neurotoxicity was not thought either to be associated with brown snake envenomation. More severe envenoming was characterised by collapse or hypotension (34; 28%), thrombotic microangiopathy (12; 10%), major haemorrhage (5; 4%), cardiac arrest (8; 7%) and death (5; 4%). The median peak venom concentration in 118 envenomed patients with pre-antivenom blood available was 1.5 ng/mL (interquartile range: 0.5 to 5 ng/mL; range 0 to 210 ng/mL). Two patients with mild envenoming had undetectable venom concentrations. One hundred and fourteen (93%) received antivenom and had post-antivenom blood concentrations, median initial dose 2 vials (IQR: 2 to 4 vials, Range 0–40). Low venom concentrations were detected post-antivenom in 2 patients who had undetectable antivenom or low antivenom concentrations. Eighteen patients received one vial of antivenom. **Conclusion:** Envenoming by brown snakes causes VICC and over 10% of patients had serious complications including haemorrhage, collapse/seizure and microangiopathy. These results plus accumulating evidence support that one vial of antivenom appears to be sufficient to bind all free venom in brown snake envenoming.

## 22. Ischemic Stroke Induced by *Bothrops lanceolatus* Envenomation: A Need for New Treatment Approaches

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**Objective:** All snake bites in Martinique, France, are due to *Bothrops lanceolatus* (BL), which may specifically result in thrombotic strokes. No other *viperidae* seems to be responsible for such neurological complications, except *Bothrops caribbeus* found in St. Lucia. Its pathophysiology is still not well established. However, despite the availability of an efficient specific antivenom (Bothrofav<sup>®</sup>), cases of thrombotic stroke are still observed. Our aims were to determine the incidence, features, and outcome of stroke following BL bites and determine its risk factors. **Methods:** We conducted a prospective observational study including 107 hospitalized patients with BL envenomation from February 2000 to January 2010. We determined the risk factors of BL-related brain stroke using a multivariate analysis. **Results:** Nine patients developed an ischemic stroke including six patients who received Bothrofav<sup>®</sup> in the first 6 hours following BL bite. Fifty-five percent of BL bite-related strokes were observed in September. In these patients, bites more frequently occurred in the upper limbs. Not all lesions were clinically symptomatic. Cardiovascular complications with a significant elevation of troponin were significantly present in association with brain damage. Magnetic resonance imaging (MRI) pattern was characteristic, constantly showing a junctional stroke predominating in the region of the posterior cerebral arteries. Final prognosis was good with satisfactory functional outcome. Using a multivariate analysis, the presence of disseminated intravascular coagulopathy was significantly related to the occurrence of stroke. **Conclusion:** Ischemic stroke following BL envenomation remains frequent despite antivenom administration. A specific

mechanism has been hypothesized in relation to diffuse thrombotic micro-angiopathy affecting the small vessels. Elevated troponin level appears to be a key indicator to perform cerebral MRI. Initial coagulopathy should alert to the risk of secondary neurological events and patients should be given maximum doses of Bothrofav<sup>®</sup>. So far, a new anti-venom serum has been marketed, showing positive results. To date, seven patients have received it without complications. **Reference:** 1. Thomas L, Chausson N, Uzan J, et al. 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.

## 23. Management of Viper Envenomation in Europe

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**Introduction:** Several species of vipers of the genus *Vipera*, *Macrovipera* or *Montivipera* live in Europe. *Vipera berus*, *Vammodytes* and *Vaspis* are the 3 species which cause the highest number of human envenomations in this continent.<sup>1</sup> Recent epidemiological data suggest that every year in the whole of Europe (including European Turkey and Russia up to the Urals and the Caucasus, representing 750 million people) around 7500 viper bites occur including approximately 1000 severe envenomations and less than 5 deaths.<sup>2</sup> As the clinical features of viper envenomation are relatively homogenous through Europe, the gradation table published in 1992 by the Pasteur Institute of Paris<sup>3</sup> is considered as pertinent for evaluating the viper bite severity at the continental level<sup>1,2</sup>. **Methods:** In order to describe the treatment protocols proposed in Europe for the medical management of viper bites, an analysis of the literature was performed. **Results:** Management of viper bites must follow strict rules both at the scene of the strike and during transportation to the hospital. First aid at the scene immediately after the bite: Immobilize the victim so as not to spread the venom. If the bite takes place in a remote area, the victim can be carried (children) or left at the scene (preferably in the company of another person). Remove tight clothing and jewelry to avoid compression due to swelling, and disinfect the wound. A loose fitting bandage may be applied from the root to the tip of the affected limb in order to impede spreading of the venom. There should be enough space for a finger between the skin and bandage. When in doubt about the ability to apply bandaging properly, it is better to do nothing than to risk creating an ischemic effect. What not to do: Do not restrict circulation by applying a tight band or tourniquet. Do not promote spread by administering drinks that increase heart rate (coffee or tea), performing mutilating acts such as wound incisions, suctioning, or cauterization. Antivenom should not be administered without medical supervision. What is not useful: Immediate use of heparin or its derivatives is unnecessary. Injection of low-molecular weight heparin may promote spread of venom. Similarly, administration of corticosteroids is not useful. Suction devices cannot extract venom injected under pressure. Management during transportation to the hospital: The presence of any local manifestation indicates grade 1 envenomation and requires hospitalization. Placement of an intravenous line is a necessary precaution to allow immediate vascular filling by macromolecules in case of arterial hypotension. Analgesics should be admin-

istered to patients in case of severe pain. Management at the hospital: Prompt clinical assessment is necessary to establish envenomation grade upon arrival at the hospital. Thorough laboratory testing should be carried out including hemogram, hemostasis and kidney functional testing. If the patient presents grade 0 envenomation, a 4-hour observation period in the emergency room may be proposed. If the patient presents grade 1 envenomation symptoms, hospitalization is required for at least 24 hours with appropriate supportive treatments: analgesics, raising and immobilizing the extremity. Antibiotics should be administered only if infection is suspected. If the patient presents grade 2 or 3 envenomation, it is necessary to undertake the only specific treatment with proven effectiveness, i.e. intravenous immunotherapy with antivenom. Quantities of required antivenom depend not on the victim but rather on the quantity and quality of the venom injected which varies depending on the age and health of the snake as well as on the season and circumstances in which the bite occurs. The pediatric dosage of antivenom is the same as in adults and only the volume of saline used to dilute the antivenom changes. Prompt use of antivenom is recommended for pregnant women in order to neutralize circulating venom that may be toxic for the placenta. Preventing the life-threatening effects of envenomation takes priority over the risk of an anaphylactic reaction which is always manageable in a properly-equipped hospital setting. Infection after snakebite, regardless of clinical envenomation grade, is a slight but non-negligible risk. However there is no consensus on the need for systematic antibacterial therapy. If antibiotic therapy is not undertaken immediately, it is important to monitor the wound site so that treatment can be started at the first sign of infection. Anticoagulant treatment using heparin or low-molecular weight derivatives is necessary in only two cases: the first indication is to prevent possible venous thrombosis in patients presenting with snakebites located on the lower extremity with extensive edema requiring prolonged decubitus; the second indication for anticoagulant treatment involves patients presenting grade 3 envenomation with disseminated intravascular syndrome. The role of surgery is limited and currently subject to controversy. In the past fasciotomy was recommended in cases involving extensive edema in order to relieve pressure and avoid peripheral ischemia due to compression. Current experience has demonstrated that immunotherapy leads to prompt reduction in edema. Peripheral ischemia was not observed in any patient included in a recent series of snakebites attributed to European vipers with or without antivenom immunotherapy. Thus fasciotomy is generally considered as unnecessary for viper envenomation in Europe and used only in cases of snakebites by other species (genus *Crotalus*). **Conclusion:** Viper bites are at the origin of relatively rare medical emergencies in Europe, but systemic poisonings with life-threatening complications are possible. Local symptomatic treatments are always prescribed but there is still an important heterogeneity in the use of specific antivenoms due to the variable antidotes availability in the different European countries.<sup>2</sup> As immunotherapy with infusion by intravenous route of purified antibody fragments is now considered as efficient and safe, antivenom treatment should be proposed to treat all moderate to severe European viper envenomation. **References:** 1. de Haro L, Glaizal M, Tichadou L, et al. Asp viper (*Vipera aspis*) envenomation: experience of the Marseille Poison Centre from 1996 to 2008. *Toxins* (Basel) 2009; 1:100–12. 2. Chippaux JP. Epidemiology of snakebites in Europe: a systematic review of

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#### 24. Impact of Comprehensive Urine Drug Screens on the Management of Poisoned Patients

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**Objective:** Urine drug screens are commonly requested in overdose patients in the belief that it will assist in patient management. Controversies continue to exist regarding the value of urine drug screening in the clinical setting. This study evaluated the clinical usefulness of the information obtained from comprehensive urine drug screens in the management of patients admitted with drug overdose. **Methods:** Urine samples were collected from patients with a diagnosis of poisoning admitted to the Prince of Wales Hospital Poison Treatment Centre (PWHPTC), a tertiary referral centre for poisoning management in Hong Kong. Drug screens were performed by liquid chromatography time-of-flight mass spectrometry and enzyme immunoassay. Patients were treated according to the protocols of the PWHPTC as clinically indicated. All patients had their serum paracetamol measured. The patient records were independently reviewed by two physicians to assess whether availability of the urine results at the time of treatment would have altered clinical management. **Results:** Urine samples were collected from 87 patients admitted to PWHPTC from January to June 2011. The mean age of patients was 38 years (range 19–106 years) and 62% were female. All except two patients recovered after standard investigations and management, which did not include knowledge of urinary drug screen results. Two hundred and forty compounds were detected in the 87 urine samples. Nine patients had no drug detected in their urine samples, while 78 patients had more than one drug detected, with a median of 2 drugs per patient. Seventy-one drugs, in 32 patients, were identified that the patients did not report taking. Of these, chlorpheniramine (7%), codeine (7%), and methamphetamine (7%) were the most common. Urine drug screens identified an additional 71 drugs not reported by patients, but earlier knowledge of them would not have affected the management or outcome of any patient. **Conclusion:** Management of overdose patients should be based on clinical symptoms and signs with directed investigations. Routine use of urine drug screens on overdose patients has limited impact on their clinical management and outcomes.

#### 25. Analysis of Drugs of Abuse in Urine Using Turbulent Flow LC-MSn

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**Objective:** Drugs of abuse may be detected and identified in urine using a number of analytical techniques, including immunoassays, LC-MS<sup>1</sup> or GC-MS<sup>2</sup>. Immunoassays tend not to be specific for the detection of individual drugs or metabolites. Current LC-MS or GC-MS methods either involve laborious sample preparation or, if sample preparation is simplified (e.g. 'dilute and shoot'), are subject to significant matrix effects. On-line turbulent flow chromatography with LC-MS is capable of detecting a number of drugs and metabolites, including many newly-

available 'designer drugs', which immunoassay cannot detect. **Methods:** An Aria TLX-I system coupled with a LCQ Fleet MS (both ThermoFisher Scientific) was used. Internal standard (25 microlitres, 20 mg/L each aqueous morphine-D<sub>6</sub>, benzoylecgonine-D<sub>3</sub>, and methadone-D<sub>3</sub>) was added to centrifuged urine samples (975 microlitres), and after mixing a portion (100 microlitres) was analysed directly using TurboFlow<sup>TM</sup> LC-MS<sup>n</sup> [TurboFlow column: Cyclone MAX 50 × 0.5 mm; analytical column: Luna PFP(2) 50 × 2.0 mm (Phenomenex)]. Analytes were detected using Data Dependent MS<sup>n</sup> scanning and identified using library matching (ToxID, ThermoFisher). Total analysis time was 20 minutes. **Results:** A range of drugs and metabolites were detected and identified using this method, including conjugated metabolites such as morphine and codeine glucuronides, lower concentration metabolites (e.g. 6-monoacetyl-morphine at 10 micrograms/L), and various amfetamines including a number of 'designer drugs' such as mephedrone. **Conclusion:** This method offers a rapid, simple analysis for drugs of abuse in urine. Operator input is minimised compared to published methods. The method is used routinely in our laboratory (i) to detect illicit drug use and (ii) for monitoring patients on programmes for the treatment of opiate addiction. **References:** 1. Duxbury K, Romagnoli C, Anderson M, et al. Development of a clinically relevant liquid chromatography tandem mass spectrometry assay for 13 drugs of abuse in urine, designed to meet the needs of the service users. *Ann Clin Biochem* 2010; 47:415–22. 2. Strano-Rossi S, Bermejo AM, de la Torre X, et al. Fast GC-MS method for the simultaneous screening of THC-COOH, cocaine, opiates and analogues including buprenorphine and fentanyl, and their metabolites in urine. *Anal Bioanal Chem* 2011; 399:1623–30.

#### 26. Drug Testing Among Hospitalized Inmates: Drug Trafficking in Prisons is a Reality

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**Objective:** Drug trafficking in jail is known but few studies have really demonstrated the extent of this phenomenon. In France physicians are never aware of the criminal file of the patients and the prison is never aware of the pathologies of the detainees. Eight specialized hospital units have been created since 2000 to ensure good health support for inmates in a secure environment. The Bordeaux Unit (UHSI) is one of these units, and inmates from three administrative French regional areas (Aquitaine, Limousin, Poitou-Charentes) can be hospitalized here. Approximately 6000 persons are annually detained in the 20 prisons in these areas of which about 400 patients are annually admitted to our unit. As drugs can interfere with some treatments, especially with anaesthetics, we systematically screen drugs in urine in all patients who are admitted to our unit. **Methods:** This is a compilation of all the measures carried out between June, 6th 2011 and September 19th 2011. All patients were screened with the exception of those who refused. Variables included origin of detention (prison, penitentiary), drugs measured by cloned enzyme donor immunoassay (cannabis, cocaine, amphetamines, opioids, buprenorphine) and treatment prescribed to determine if positive opioid detection was linked to a prescribed treatment. **Results:** 138 patients were hospitalized in UHSI between June, 6th 2011 and September 19th 2011. In 18 screening was not

performed; in 3 of these the patients refused. Among the 120 remaining urine samples some were positive for cannabis (19), opioids except methadone and buprenorphine (10) and buprenorphine (8). Two patients were not on buprenorphine when admitted to the unit, and all patients positive for opioids were under prescribed treatment of tramadol or morphine. **Conclusion:** Despite only a fraction of detainees of the three areas being hospitalized in our unit, we can conclude that drug trafficking remains a problem in 2011. Cannabis remains the most popular drug in jail and no cocaine or amphetamine, including ecstasy, was notified.

#### 27. Analytical Strategy for Identification, Determination and Confirmation of Valproic Acid in Suspected Case of Drug Misused in a Child

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**Objective:** The aim of the study was to identify, measure and confirm the presence of valproic acid in different biological samples (urine, blood, hair) from a 14-month-old baby, suspected of accidental drug misuse. Different analytical strategies and instrumental techniques were applied in order to analyze the drug and to confirm its presence. **Methods:** Before admission, a urine sample was tested using immunochemistry (benzodiazepines, barbiturates, tricyclic antidepressants, opiates, methadone, and cocaine) and GC-MS analysis (on HP-5ms capillary column), after basic and neutral liquid-liquid extraction. Confirmation was made using derivatization step (silylation with BSTFA) and HPLC-UV (as 4-bromophenacyl ester, on ODS-column). The quantitative analyses in blood serum were performed on GC-FID (carbowax capillary column, neutral liquid-liquid extraction with ethyl acetate, without derivatization and 1,3-propanediol as internal standard). The confused and discrepant case history (visits in kindergarten and somnolence after that) necessitated additional analysis to be performed. Hair sample was tested (GC-MS analysis after methanol extraction) three months later. **Results:** General toxicology screening and GC-MS analyses of the urine identified the presence of valproic acid. Confirmation analysis using derivatization step and independent analytical method confirmed the presence of the drug and the parents were referred for consult to the Toxicology Clinic. The baby was admitted to the children's unit with impaired general status – presence of cerebrotoxic signs (somnolent, apathetic). The laboratory findings (complete blood count, clinical chemistry and blood gases) were in the reference range. Toxicological analysis found 2.2 micrograms/mL valproic acid in blood. The child was somnolent for the next 24 h after admission, then recovered and was discharged on the third day after admission in his usual status. The doubts around drug presence in the child enforced additional hair-testing, which definitely confirmed the presence of valproic acid. In the hair concentration was 7.6 micrograms/g. **Conclusion:** The application of different analytical strategies, methods and techniques is important in unclear and potentially forensic cases, when the analytical result is important. Although valproic acid is a volatile and unstable drug, it is possible to find it in hair three months later. The variety of analytical techniques and application of hair analyses is illustrated as an additional confirmation step.

### 28. Adequacy of a Laboratory Therapeutic and Illicit Drugs Test Directory of a Clinical Toxicology Laboratory Based on the Recording of Acute Overdose Patients

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**Objective:** To provide safe care for intoxicated patients, Emergency Departments (ED) should know the exact profile of attending poisonings in order to adapt their diagnostic laboratory resources. The objective is to know which therapeutic and illicit drugs are most prevalent in our population and determine which of them we can identify and quantify with our current analytical technology. **Methods:** We analyzed the frequency of intoxications secondary to therapeutic and illicit drugs in our ED with a high frequency of presentation (> 1.00%) by means of a study of our database during three years (2007–2009). Patients were older than 15 years of age. The knowledge of drugs implicated in acute poisoning is based on self-reporting by the user or their companions and these were not necessarily confirmed by laboratory testing in all cases. **Results:** 2571 cases of therapeutic and illicit drugs were implicated in the registered intoxications. Sixteen of these drugs fulfilled the criteria of frequency (> 1.00%), four illicit drugs: cocaine (13.7%), heroin (3.53%), cannabis (2.83%), amphetamines (1.24%) and twelve therapeutic drugs: benzodiazepines (33.6%), paracetamol (2.76%), ibuprofen (2.48%), venlafaxine (1.63%), quetiapine (1.59%), mirtazapine (1.47%), trazodone (1.43%), digoxin (1.32%), zolpidem (1.24%) metazolol (10.8%), escitalopram (1.08%) and methadone (1.05%). In 56.2% of cases, our laboratory was able to quantify (18.7%) or identify (37.5%) the therapeutic or illicit drugs, but in 43.8% of the poisonings we were not able to perform these analyses: 4 non-tricyclic antidepressants (venlafaxine, mirtazapine, trazodone, escitalopram), 2 analgesics (ibuprofen, metazolol) and one psychotropic drug (zolpidem). **Conclusion:** Benzodiazepines and cocaine are the main etiology of intoxications caused by therapeutic and illicit drug respectively. Both are determined qualitatively in urine by our laboratory. Non-tricyclic antidepressants, analgesics and some psychotropic drugs are the main groups of therapeutics drugs that our laboratory has to make an effort to adapt the analytical techniques to our local prevalence of acute intoxications. **Reference:** 1. Wu AH, McKay C, Broussard LA, et al. National academy of clinical biochemistry laboratory medicine practice guidelines: recommendations for the use of laboratory tests to support poisoned patients who present to the emergency department. Clin Chem 2003; 49:357–79.

### 29. Detection of Benzodiazepines and Metabolites in Urine Using Turbulent Flow LC-MS/MS

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**Objective:** Generally illicit benzodiazepine use is part of a polydrug abuse pattern.<sup>1</sup> Use as 'legal highs' has also been reported.<sup>2</sup> Aims of urinalysis are assessing adherence to prescribed medication and detecting additional illicit benzodiazepine use. Immunoassays can only detect benzodiazepines by class as opposed to individual

compounds, whilst TLC and GC-MS require hydrolysis and/or derivatisation steps, and even then are often only 'group specific'. Use of LC-MS/MS enables direct analysis of urine and gives specific identification of even conjugated metabolites. **Methods:** An Aria Transcend™ TLX-II coupled with a TSQ Vantage™ MS was used (ThermoFisher Scientific). Centrifuged urine samples (100 µL) were mixed with aqueous internal standard solution (diazepam-D<sub>5</sub> and oxazepam-D<sub>5</sub>, 100 µL) and deionised water (800 µL). A portion (50 µL) of the mixture was directly analysed by TurboFlow™ LC-MS/MS (50 × 0.5 mm Cyclone-P TurboFlow column, 50 × 2.1 mm Hypersil GOLD C18 analytical column). Analytes were eluted using a methanol:water gradient and detected using SRM (2 transitions per analyte, positive ESI, <sup>37</sup>Cl ratio confirmation where possible). **Results:** Total analysis time was 10 minutes for 13 benzodiazepine drugs/metabolites. Accuracy (%) and precision (% RSD) were 88–115% and < 18% for all analytes, respectively. Additional peaks were observed in extracted SRM chromatograms from samples from patients prescribed oxazepam and temazepam. These were found to be consistent with glucuronide conjugates undergoing in-source loss of the conjugate moiety ([M-C<sub>6</sub>H<sub>5</sub>O<sub>7</sub> + H]<sup>+</sup>). **Conclusion:** TurboFlow LC-MS/MS enables rapid, direct analysis of benzodiazepines and metabolites in urine. The method possesses good sensitivity for analytes that are normally present in low concentration such as 7-aminoclonazepam, an important consideration if covert benzodiazepine administration is suspected as in drug facilitated sexual assault. Analysis of an EQA sample containing 7-aminoclonazepam (116 µg/L) gave a positive result; of 217 laboratories, only 3 reported a positive result for this sample (UKNEQAS). **References:** 1. Darke S, Hall W. Levels and correlates of polydrug use among heroin users and regular amphetamine users. Drug Alcohol Depend 1995; 39:231–5. 2. Maskell P, De Paoli G, Seetohul N, et al. Phenazepam is currently being misused in the UK. BMJ 2011; 343:d4207.

### 30. Assessment of Overall Toxicity of Different Illicit Drugs

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**Objective:** To create a simple tool to be able to evaluate the overall toxicity of different illicit drugs with the focus on harm to the user. Physicians and pharmacists may be advised by legal authorities to evaluate the toxicity of different illicit drugs from a legal perspective. There is no consensus on how to compare toxicity of different drugs. New drugs are difficult to evaluate and judge in terms of general toxicity. **Methods:** We interviewed a physician, a professor in social medicine, a police officer working with narcotics, and a previous abuser of narcotics to decide which medical and social risk factors should be included in a scoring sheet. We assessed 19 different substances of abuse after collecting and studying at least ten scientific reports from peer reviewed journals on every drug. **Results:** A scoring sheet was created where each drug could be evaluated in eleven different aspects of toxicity from zero to five points (six-graded). Some parameters were assessed to carry higher impact for overall toxicity than others and were therefore multiplied by three. The parameters assessed were the following with risk for: substance dependence, chronic abuse, life threatening overdose, death due to abuse (not acute overdose), multiple drug abuse, acute psychiatric episode, psychiatric long-term sequelae, somatic disease, alcoholism, trauma,

and criminality. **Discussion:** The different aspects of overall toxicity may be categorized as acute (I-IV), long-term consequences (V-IX) and accumulated aspects. We believe that acute toxicity has a higher impact on overall toxicity than long-term consequences and accumulated aspects since it is prompt and an early death due to acute toxicity eliminates any long-term effects. **Conclusion:** This scoring system allows a comparison of different drugs in terms of overall toxicity. It takes into account several different medical and social parameters giving a reasonable judgment of overall toxicity for each drug.

### 31. Gamma-Butyrolactone Criminal Poisoning with Multidisciplinary Investigations in a Medico Legal Department: A Case Report

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**Objective:** Gamma-butyrolactone (GBL)/gamma-hydroxybutyrate (GHB) poisoning is rarely proved with biological analysis and early sampling is essential. We present a case of criminal poisoning where the victim was admitted to a specialised medico-legal unit for victims of aggression. The multidisciplinary investigation (doctors, toxicological laboratory) permitted making an early adequate medical examination, sampling and analysis to prove GHB poisoning. **Case report:** A 22-year-old young man woke up at 6.30 am in an outside car park, complaining of violent anal pains, headaches and short term memory loss. He found a flask containing a liquid near him, which he showed to emergency services. He was sent to the emergency room and several blood and urine samples were collected, at 7.50 am, on the advices of the forensic scientist. Because of the suspicion of a chemical criminal poisoning, other samples for toxicological and biomolecular analyses were collected. **Results:** Toxicological screening was realized with the ELISA method, and showed the presence of blood paracetamol in the therapeutic range but neither alcohol nor any other medicine or drug. In urine GHB was brought to light by gas chromatography/mass spectrometry, at a rate of 12 µg/mL. Doses measured in the urine indicated that substances had been taken within the last 10 hours. The contents of the flask showed the presence of 99.9% GBL and 0.1% GHB. **Conclusion:** In this case of GBL/GHB poisoning, substances were detected in urine because samples were taken rapidly after the crime. As GBL hydrolysis to GHB occurs they both disappear quickly from blood and urine (less than 10 hours from urine), and they are rarely detected. It is important to underline the need for quick examination, sampling and analysis. In this case it was possible because the victim was brought to a specialised medico-legal unit for victims of aggression where forensic scientists are trained for this kind of situation.

### 32. A Rare Use of Pesticide Poisoning as an Adjunct to Homicidal Hanging

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**Objective:** Homicide by hanging is very rare. In India, several cases have been reported wherein a victim was first murdered and later on suspended to simulate suicidal hanging or in which a person rendered sense-

less was hanged later on. A common aspect of such homicides is the use of a poisonous substance or stupefying agent before the actual murder to prevent any form of resistance by the victim. Alcoholic beverages are commonly used for the above purpose. *Case report:* The reported case involves use of the organo-phosphorus pesticide parathion admixed with alcohol as an adjunct to murder. A youth belonging to the Sikh religion was found hanging by his turban in a well. A blanket was thrown over his face and shoulders which was stained with vomit. The case was referred to our department for expert post-mortem examination. A thorough autopsy was carried out; the injuries noted and viscera sent for chemical analysis. The injuries were typical of neck constriction on account of ante-mortem hanging. The ligating material had a sliding knot, typical of hanging. The viscera, clothes, pagri (turban) and the bed sheet were positive for both ethyl alcohol and organo-phosphorus pesticides. The blood alcohol concentration as reported by Forensic Science Laboratory analysis was 0.18–0.30 g/100 mL. The organo-phosphorus pesticide parathion was detected by qualitative chemical analysis with a mean level of 0.03 mg/mL (stomach, liver, spleen and kidneys being analyzed). *Conclusion:* According to Indian estimates, pesticides are responsible for around 76,000 deaths annually with organo-phosphorus pesticides and aluminum phosphide topping the list. The majority of such deaths are accidental, suicidal manner following next. Homicides by pesticide poisoning are rare. The reported case was a rare combination of pesticide poisoning followed by homicidal hanging. *References:* 1. Vijayakumar S, Fareedullah Md, Sudhakar Y, et al. Current review on organophosphorus poisoning. *Arch Appl Sci Res* 2010; 2:199–215. 2. Kumar L, Agarwal SS, Chavali KH, et al. Homicide by organophosphorus compound poisoning: a case report. *Med Sci Law* 2009; 49:136–8.

### 33. Does Handling E85 Motor Fuel Produce Positive Breath Alcohol Readings?

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*Objective:* To determine whether handling E85 fuel (85% ethanol, 15% gasoline) produces measurable breath alcohol using a handheld analyzer. *Methods:* We recruited 5 healthy adult volunteers in an IRB-approved study conducted at a commercial gas station. Before each trial, each subject affirmed a minimum of 24 hours of abstinence from drinking alcoholic beverages and was tested with the BACTrack S50 handheld breath alcohol analyzer (KHN Solutions, San Francisco CA) to confirm a blood EtOH concentration (BAC) of 0.00% (0 mg/dL). Then each handled a minimum of 8 US gallons (30 liters) of E85 fuel under each of 4 scenarios: A) from fuel pump to car, B) from pump to gas can, C) from gas can to another gas can, and D) from gas can to car. We measured BAC at 0, 2, 4, 6, 8, 10, 15, 20 minutes after each fuel handling procedure. Trials occurred on different study days. Alcohol concentrations are expressed in whole blood concentrations in % EtOH (or g/dL) using the conversion of 210 L of breath = 100 mL of blood. *Results:* In scenario A, all subjects had BAC of zero at all times. In scenario B, 1 subject had a single BAC of 0.02% at 2 minutes; all other readings were 0. In scenario C, 2 subjects had measurable BAC of 0.04% and 0.02% at 0 minutes followed by BAC of 0 for all subsequent readings. In scenario D, 2 subjects had measurable BAC including 1 subject with 0.02% at 2 minutes and 0.01% at 6 minutes (with a 0 reading

at 4 min) and 1 subject with a single reading of 0.01% at 4 min. No subject had a BAC greater than 0.04% at any time. All BACs were 0.00% in all subjects after 6 min. *Conclusion:* Handling E85 motor fuel produced low, transient elevations in breath alcohol measurement up to 6 minutes in a minority of subjects. Standard police procedures include 15 minutes after a traffic stop before administering a breath alcohol test. It is unlikely that handling E85 motor fuel prior to arrest would result in erroneous prosecution for driving while intoxicated.

### 34. Does Therapeutic Use of Tapentadol Produce a False Positive Urine Drug Screen for Amphetamine?

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*Objective:* To determine whether therapeutic use of tapentadol is associated with false positive urine screen for amphetamine by immunoassay. Tapentadol (Nucynta®, Janssen Pharmaceuticals, Titusville NJ), is a newer, synthetic analgesic approved in the US in 2008. Although mechanisms of action include mu opioid receptor agonism and serotonin reuptake inhibition, the drug is structurally similar to amphetamine. *Methods:* We recruited patients from a pain management clinic and a rheumatology clinic into an IRB-approved study. We screened computerized clinic records to identify patients with upcoming appointments who had recorded prescriptions for tapentadol. We met all eligible patients on their scheduled appointment days and explained the purpose of the study. We excluded patients who were taking prescription amphetamines or bupropion, who admitted illicit amphetamine use, or who had not taken tapentadol in the three days before screening. Screened patients were allowed to opt out without stating a reason. Enrolled patients then provided a spontaneously voided urine specimen which we tested using the Siemens Syva EMIT II immunoassay. All positive results would then be confirmed by thin-layer chromatography. We recorded each patient's prescribed dose and asked patients to report the number of doses taken on the study day and the two preceding days. *Results:* We screened 21 patients taking tapentadol. We excluded 10 patients (3 had not taken the drug recently, 2 had excluding medications, 2 did not show to their appointments, 2 declined, 1 researcher unavailable). We enrolled 11 patients (8 women, 3 men) with ages ranging from 31 to 86 years (mean 49.5, median 50). Daily dose ranged from 50 to 600 mg/day (mean 268 mg/day, median 200 mg/day). All urine specimens produced a negative immunoassay result for amphetamine in all 11 patients. *Conclusion:* Therapeutic use of tapentadol up to the maximum dose of 600 mg/day did not produce a false positive urine amphetamine screen using the Siemens Syva EMIT II immunoassay.

### 35. Epidemiology of Viper Bite Poisoning in the Italian Region Emilia Romagna and Efficacy of Treatment with Antibody Fragments

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*Objective:* The Regional Reference Center for the supply of antidotes (CRR) is located in the Department of

Pharmacy of the University Hospital of Ferrara. The center has the only regional allocation of antibody fragments of equine origin, for treatment of snake bites. The antidote supplied is able to bind and inactivate the toxins of the venom of different species of European vipers, such as: *V. ammodytes*, *V. aspis*, *V. berus*, *V. ursini*, *V. xanthine*, *V. labetina*. Emilia Romagna (ER) is a region with a diverse geography and also includes mountainous areas with an average altitude over 1000 meters. In the ER, only *Vipera aspis* is common (information from the State Forestry Corps), up to an altitude of 1400 meters and in coastal pine forests. *Vipera aspis* is often found near to inhabited areas. In case of bites with injection of venom there can be significant neurotoxic symptoms. The purpose of this study is to describe the use of viper venom-specific antibody in ER in the years 2010–2011 according to the symptoms presented by patients. *Methods:* CCR has recorded cases of snake bite occurred in the ER from 01/01/2010 to 30/10/2011. The epidemiology of intoxicated patients, the number of treatments with antidotes and how these have changed the severity of intoxication have all been evaluated. *Results:* The CRR has analyzed 11 cases of viper bite poisoning; in only 1 case was the viper identified; in 25% of cases it was pediatric patients. 37.5% of those intoxicated showed only signs of the bite, 25% local edema, 12.5% local and systemic edema signs or mild symptoms, 25% severe local and systemic events targeting the vascular system. In no case were neurotoxic symptoms reported. Antidote treatment was administered in 27% (3/11) of envenomations. *Conclusion:* In this study the use of the viper venom-specific antibodies was limited as it is reserved for patients with severe systemic symptoms. No adverse reaction was found after administration of the antidote. There were no neurotoxic symptoms.

### 36. Elevated Compartment Pressures from Copperhead Envenomation Successfully Treated with Antivenom: A Case Report

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*Objective:* *Crotalinae* envenomation causes profound local soft tissue effects; however, compartment syndrome is rare because swelling is usually confined to the subcutaneous tissue.<sup>1</sup> Fasciotomy has been the traditional approach to compartment syndrome, although existing surgical data often predates the availability of effective antivenom. Animal models and human case reports suggest elevated compartment pressures from snake envenomation can be treated non-surgically with antivenom.<sup>1</sup> We report a case of a 17 month-old with elevated compartment pressures successfully treated with antivenom alone. *Case report:* A 17 month-old female sustained a copperhead bite to the foot and presented to the emergency department with circumferential edema, erythema, and ecchymosis of the foot and distal ankle. The patient had palpable pulses and was neurologically intact on presentation. Initial laboratory studies: PT 11.4s, PTT 25.4s, INR 1.1, FDP ≤ 5 micrograms/mL, CPK 230IU/L, platelets 310,000/μL. Due to the significant soft tissue effects, the child received an initial dose of 4 vials of Crotaline Polyvalent Immune Fab. Within 10 hours of the first dose, the patient's edema extended to the groin, with maintained sensation and dopplerable pulses. Compartment pressures of the extremity were measured as follows: anterior 85 mmHg, lateral 55 mmHg, posterior 27 mmHg, deep posterior 34 mmHg,

foot 60 mmHg, quadriceps 30 mmHg. Fasciotomy was deferred and the patient received an additional 6 vials of antivenom, followed by 2 additional 6 vial doses. Repeat compartment pressures: 54 mmHg anterior, 30 mmHg lateral. There was a 2.2 cm mean decrease in limb diameter within 48 hours of the first pressure measurement. The patient was put on maintenance dosing and ultimately received a total of 26 vials of antivenom. The patient did not develop significant coagulopathy or thrombocytopenia. Swelling continued to improve with return of limb function. **Conclusion:** Compartment syndrome is a rare complication of *Crotalinae* envenomation. Data regarding the role of fasciotomy in the treatment of elevated compartment pressures due to snake envenomation is limited. Early and aggressive treatment with antivenom may avoid invasive fasciotomy and should be considered in patients with *Crotalinae* envenomation and significantly elevated compartment pressures. **Reference:** 1. Cumpston KL. Is there a role for fasciotomy in *Crotalinae* envenomations in North America? *Clin Toxicol (Phila)* 2011; 49:351–65.

### 37. Managing Cases of Envenomation in Resource Limited Health Care Settings: Tamilnadu Model

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**Objectives:** To highlight the status of treating cases of envenomation (snake bite and scorpion sting) in Government primary health care centres [first referral unit] and secondary health care hospitals [taluk level], and to stress the training of doctors and nurses. **Methods:** Existing status along with personal fear and apprehension about treating cases of envenomation in 1306 primary health care centres [PHCs] and 553 secondary health care hospitals were elicited through a questionnaire survey, and analysed in relation to doctor, drugs, devices and directions. Data were analysed statistically. **Results:** Health care team, drugs, and directions were adequate in all these centres. Of them, 270 doctors and 540 nurses of 33 centres were trained under Phase I to handle various poisoning cases including bites and stings. They were provided with devices, and treated 23,525 snake bites (SB) and 9,899 scorpion stings (SS) between April 2009 and September 2011. Before training, diagnostic capabilities, knowledge on referral, therapeutic aspects, ability to handle cases and care givers, and documentation and reporting were satisfactory among 88, 60, 56, 45 and 8% respectively. After training of doctors and nurses of these 33 centres with respect to diagnosis, referral, medico legal aspects, counselling and management of these cases, referral and death rate came down to 3.7 and 1.2% respectively. Policies were made for uninterrupted supply of drugs and devices by the Government of Tamilnadu. **Conclusions:** Participation of policy makers and professional involvement in the treatment of snake bite and scorpion sting cases have reduced the morbidity, mortality and referral. Thus the Tamilnadu model is working well consistently. **Reference:** 1. Handbook on Treatment Guidelines for Snake Bite and Scorpion Sting 2008 TNHSP Publication. <http://www.free-books.us/Others/52115/ Handbook-on-Treatment-Guidelines-for-Snake-Bite-and-Scorpion-Sting-2008-TNHSP-Publication> [accessed 18 Feb 2012].

### 38. Bites in Australian Snake Handlers – Australian Snakebite Project (ASP-15)

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**Objective:** Snakebites in snake handlers are an important clinical problem that may differ to bites in the general population. The aim of this study was to investigate the epidemiology and clinical presentation of bites in snake handlers. **Methods:** Bites in snake handlers recruited as part of the Australian Snakebite Project (ASP) from 2004 to 2011 were included in the study. Data were extracted from the ASP database, which included demographic and clinical information, laboratory tests and antivenom treatment. **Results:** From 1042 snake bites recruited to ASP, there were 108 (10.4%) bites in snake handlers, including three patients bitten on three different occasions, seven patients bitten on two occasions and one 21 month old boy bitten by his parent's snake. The median age was 40 y (1 to 81 y) and 105 (97%) were males. The commonest circumstances of the bites were handling snakes (37), catching snakes (30), feeding snakes (16), cleaning cages (11), medicating snakes (2) and milking a snake (1). Alcohol was involved in 9 cases (8%). Ninety four patients put on a pressure bandage (87%). Bites were from Brown snakes, *Pseudonaja spp.* (18), Tiger snakes, *Notechis spp.* (14), Red-bellied black snakes, *Pseudechis porphyriacus* (19), Mulga snakes, *P. australis* (6), Collett's snake, *P. colletti* (4), Taipans, *Oxyuranus spp.* (14), Death adders, *Acanthophis spp.* (14), *Hoplocephalus spp.* (8) and Rough-scaled snake, *Tropidechis carinatus* (2). Bites were to the upper limb in 105 cases, the lower limb in two and the abdomen in one. Envenoming occurred in 72 cases, anaphylaxis to venom in three and 33 were non-envenomed. Venom induced consumption coagulopathy was the commonest envenoming syndrome in 44 patients, followed by systemic symptoms (11), myotoxicity (8), anticoagulant coagulopathy (6) and neurotoxicity (3). Antivenom was administered in 62 patients and the majority of envenomed patients not receiving antivenom were red-bellied black snake bites. **Conclusion:** Bites in snake handlers remain a common and important problem and involve a broad range of snakes that differs from snake bites in the wild. Almost all bites were in males on the upper limb and involved handling the snake. Anaphylaxis to venom must be remembered in snake handlers.

### 39. When is Antivenom Used for Copperhead (*Agkistrodon contortrix*) Snake Bites?

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**Objective:** In 2001, *Crotalidae* Polyvalent Immune Fab (ovine) was approved in the USA for the treatment of patients with North American Crotalid envenomation. However, the use of antivenin for *Agkistrodon contortrix* (Copperhead) envenomation remains controversial. These snake bites usually cause only mild to moderate local tissue effects and rarely cause significant systemic effects. There is some evidence that antivenin

may be helpful for these patients. Our objective was to determine if the physician decision to use antivenin is affected by whether the copperhead snake bites the upper or lower extremity. **Methods:** This was a retrospective case-control study of snake bite patients who received antivenin and those who did not. We reviewed all *Agkistrodon contortrix* (copperhead) bites reported to the Texas Poison Center Network (TPCN) from 2005–2009. Inclusion criteria included all human exposures where copperhead was listed as the substance and bite/sting as the route of exposure. The cases were reviewed for gender, age, bite location on body, type of snake, and whether ovine Fab antivenin was used. Statistics used were descriptive and chi-square. **Results:** There were 389 patients with copperhead snake bites reported to the TPCN during the 5 year study period. Most were male (65.8%). Over one-fourth were under 20 years of age and only 2.6% were over 70 years. Only 222 (57.1%) received ovine FAB antivenin. Of the 227 (58.3%) patients who were bitten on an upper extremity, 144 (64.8%) received antivenin. Of the 168 patients who were bitten on a lower extremity, 78 (48.1%) received antivenin ( $p = .004$ ). There were no statistically differences for those who received antivenin for male or female (55.9% and 59.4%,  $p = .58$ ) or age range ( $p = .62$ ). **Conclusion:** This is the largest analysis of bite location of copperhead snake bite patients. The use of antivenin differs according to bite location but not for gender or age of the patient. It is not clear why physicians are more likely to use antivenin for upper extremity bites compared to lower extremity bites. Limitations of this study include the retrospective nature and accuracy of self-reported data to the poison centers.

### 40. Severe Systemic and Local Complications Associated with Green Pit Viper Bites

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**Objective:** In Hong Kong, the white-lipped green pit viper (*Trimeresurus albolabris*) accounts for the great majority of snake bites. In this retrospective study, the main objective was to determine the incidence of severe systemic and local complications following *Tr. albolabris* bites among individuals aged 18 years or older in the New Territories East Region during 1994–2008. **Methods:** With the opening of two general hospitals for the Tai Po District and North District during 1997–1999, Prince of Wales Hospital (PWH) mainly serves the Shatin District since 2000. The population size of subjects aged 18 years or older in the Shatin District was 503,498 in 2006. Subjects with snake bites (ICD codes E905.0, T63.0, X29) requiring hospitalisation in PWH during 1994–2008 were identified by searching our computerised medical record system. The medical records and/or discharge summaries were reviewed. The diagnosis of *Tr. albolabris* bites was based on description of the snake, examination of the snake captured and/or the haematological features characteristics of pit viper bites<sup>1</sup>. The presence of severe local and systemic complications, the need for surgical procedures and antivenom therapy and the outcomes were noted. **Results:** Thirty-six definite or probable cases of *Tr. albolabris* bites were studied. There were 25 males and 11 females, with a median age of 53 years (range 18–80 years). Severe coagulopathy was seen in 10 patients (28%) requiring the infusion of fresh frozen plasma with or without platelet concentrates in all patients and antivenom therapy in five patients. Severe local com-

plications were seen in three patients (8%), including a patient with severe coagulopathy. Two patients with digital gangrene (including one with severe coagulopathy) required amputation of the affected digit. One other patient had severe local oedema of the affected limb. There was no mortality. **Conclusion:** *Tr. albolabris* bites can result in severe coagulopathy and local complications such as digital gangrene. Patients should be carefully assessed and monitored. Where indicated, timely use of antivenom therapy can rapidly correct the coagulopathy and prevent local complications. **Reference:** 1. Chan TYK, Critchley JA. An epidemiological study of the snake bites in the New Territories East, Hong Kong. *Ann Trop Med Parasitol* 1994; 88:219–21.

#### 41. *Vipera berus* and *Vipera ammodytes* Bites in Slovenia: Distribution and Clinical Characteristics

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**Objective:** Three species of poisonous snakes are indigenous to Slovenia, all of the family *viperidae* (*V. berus*, *V. ammodytes* and *V. aspis*). *V. aspis* is only present in a small and mostly uninhabited area, therefore most of the poisonous snake bites are from the first two species. The aim of the study was to find differences between *V. berus* and *V. ammodytes* bites. **Methods:** Retrospective analysis of data obtained from phone calls to the national Poison Control Centre (PCC) for the period between January 1999 and December 2010. The geographic distribution of bites and grade of poisoning according to Poisoning Severity Score (PSS) were analysed. The outcome according to PSS was described as follows: no symptoms or signs, minor, moderate, and severe. **Results:** During the 12 year period 61 snake bites were registered. Victims were equal parts male and female. Eighteen bites occurred in children younger than 18 years. Most of the times victims were bitten on their limbs (27 on the hand; 19 on the leg). *V. berus* was positively identified in 13, and *V. ammodytes* in 9 cases. Most of the offending snakes remained unidentified (33) or were classified as non-poisonous or other (6). In the Mediterranean region of Slovenia *V. ammodytes* bites predominated (5:1). In the Alpine region of Slovenia 5 bites were from *V. berus* and 3 bites from *V. ammodytes*. In the remaining part of Slovenia *V. berus* bites predominated (7:1). The difference was statistically significant (Chi-Square test;  $p = 0.0278$ ). According to PSS, the consequences of *V. ammodytes* bites were mostly classified as moderate (6) or severe (1), while in *V. berus* bites they tended to be minor (10) or none (3). The difference was statistically significant (Chi-Square test;  $p = 0.0017$ ). No lethal cases were recorded. **Conclusion:** Snake bite in Slovenia is rare. *V. berus* bites are the commonest in Slovenia, but *V. ammodytes* bites are clinically more severe. Data show that *V. ammodytes* is a more aggressive species, and is also more widely distributed in the country.<sup>1</sup> **Reference:** 1. Krofel M, Cafuta V, Planinc G, et al. Distribution of reptiles in Slovenia. *Nat Slov* 2009; 11:61–99.

#### 42. Envenoming by *Vipera berus*: A Case Report of Neurotoxicity

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**Objective:** To report a case of a child bitten by the Balkan adder, *Vipera berus bosniensis* in S-W Romania, focussing on the neurotoxic manifestations. *Vipera*

*ammodytes* is well known for neurotoxic and sometimes lethal consequence after snake bite in our country. *Vipera berus* bites are not of big epidemiological significance, but in some cases life-threatening symptoms may appear. **Case report:** A healthy 14 year old girl from a rural area was bitten by an adult viper and she reported no previous snakebites. The main clinical features presented on the first day after the bite. The bite was on the right foot with a local edema, reddening and pain at the site of the bite. On admission, the girl was fully conscious. She became dizzy with sleepiness, vertigo, and disorientation. Bilateral ptosis and blurred vision developed, followed by difficulty in swallowing (with mouth open and showing the teeth). She was then admitted to the Intensive Care Unit. She did not receive antivenom. *Vipera berus bosniensis* (identified by the family) is considered to have neurotoxic venom but little evidence is available in the literature. We compared our clinical signs with those in papers already published and we found that difficulty in swallowing was not mentioned and neurotoxic manifestations appeared rarely. **Conclusion:** Clinical effects of postsynaptic neurotoxins tend to resolve more rapidly than those caused by presynaptic neurotoxins which damage the nerve terminals and this can explain the rare neurotoxic manifestations. **References:** 1. Calderón L, Lomonte B, Gutiérrez JM, et al. Biological and biochemical activities of *Vipera berus* (European viper) venom. *Toxicon* 1993; 31:743–53. 2. Harborne DJ. Emergency treatment of adder bites: case reports and literature review. *Arch Emerg Med* 1993; 10:239–43. 3. Malina T, Krecsak L, Warrell DA. Neurotoxicity and hypertension following European adder (*Vipera berus*) bites in Hungary: case report and review. *QJM* 2008; 101:801–6.

#### 43. Skin Rash, Joint Pain and Fever after Antivenin Injection for Cobra Bite: A Case Report

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**Objective:** Antivenin is the major treatment for venomous snakebites. According to a literature review, serum sickness induced by antivenin has been reported frequently in the United States, but it is seldom notified in Taiwan. Serum sickness is a type III hypersensitivity reaction mediated by deposits of circulating immune complexes from foreign antigenic materials. The reported typical signs and symptoms of serum sickness are rash, fever, malaise and polyarthralgias. We present a male patient who suffered from skin rashes, multiple joint pain and fever after antivenin therapy for cobra bite. **Case report:** A 47-year-old male was bitten by a cobra on his right thumb when working in the farm. Rapidly progressive tenderness, erythema and swelling over his right hand developed soon after the bite. A total of 9 vials of polyvalent antivenin therapy for cobra bite and empiric antibiotics for possible cellulitis were given. He suffered from an acute onset of skin rash over both limbs, severe multiple joint pain and intermittent fever 10 days after use of the antivenin. These symptoms resolved after steroid treatment. Debridement was also performed because necrosis progressed. Antivenin induced serum sickness was the likely cause. **Conclusion:** Unlike in the USA, antivenin related serum sickness is rare in Taiwan. The difference may be related to the efficacy and dosage of antivenins administered to manage venomous snakebite. We strongly recommend close observation of the effects for 2 weeks or more after use of antivenin. **References:** 1. Huang CY, Hung DZ, Chen WK. Antivenin-related serum sickness. *J Chin Med Assoc* 2010; 73:540–2. 2. Lawley TJ, Bielory L,

Gascon P, et al. A prospective clinical and immunologic analysis of patients with serum sickness. *N Eng J Med* 1984; 311:1407–13. 3. Gold BS, Dart RC, Barish RA. Bites of venomous snakes. *N Eng J Med* 2002; 347:347–56.

#### 44. Immigrant Spiders – a Cause for Concern?

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**Objective:** ‘*Steatoda nobilis*’, commonly known as the false black widow spider, is an immigrant spider originating from the Canary Islands. Closely related to the black widow species but lacking its distinctive red spot, this spider was first reported in the UK in 1879. It has since become acclimatised along the south coast of England although National Poisons Information Service (NPIS) call records indicate that it has been witnessed as far north as Yorkshire. While the spider is not considered aggressive, it possesses large venomous fangs that can instigate ‘instant’ severe pain, described as being worse than a wasp sting. **Methods:** A case study is reported and enquiries to NPIS concerning false black widow spider bites between August 2007 and August 2011 were analysed with regard to location and features. **Case report:** A 41-year-old male presented to the accident and emergency department two days after being bitten on the calf by a spider subsequently identified as ‘*Steatoda nobilis*’. He was treated prophylactically with co-amoxiclav. The skin around the bite was warm and discoloured with acute swelling at the puncture site. NPIS advised that apart from appropriate analgesia further treatment was unlikely to be required and that localised features from the envenomation would subside with time. Other than mild cellulitis in the calf and a raised CRP (31 mg/L), this patient exhibited no systemic complications and was discharged the same day. **Results:** NPIS received 21 enquiries involving ‘*Steatoda nobilis*’ throughout the study period. The majority of enquiries were from southern England with a few as far north as Yorkshire and Suffolk. Localised oedema was the most significant feature along with hypoaesthesia, paraesthesia and skin rash. Systemic features such as tachycardia, chest tightness, vomiting, anxiety with increased sweating and fever were also reported in five cases. **Conclusion:** It has been reported that ‘*Steatoda nobilis*’ bites may be neurotoxic and affect the parasympathetic nervous system.<sup>1</sup> Nevertheless, NPIS experience suggests that these bites, although sometimes medically significant, can be managed successfully with supportive care and analgesia. **Reference:** 1. Warrell DA, Shaheen J, Hilliard PD, et al. Neurotoxic envenoming by an immigrant spider (*Steatoda Nobilis*) in southern England. *Toxicon* 1991; 29:1263–5.

#### 45. Neurological Disorders after *Cotylorhiza tuberculata* Jellyfish Consumption: A Case Report

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**Objective:** Jellyfish in the Mediterranean Sea can sometimes cause painful stings, but generally they are considered to be harmless. To this group of jellyfish belongs also *Cotylorhiza tuberculata* (known as the poached egg jellyfish or cauliflower jellyfish

– it depends on your viewpoint). Poisonings resulting from sea food consumption in Slovenia are rare. They are confined to scombroid reaction after tuna fish or shellfish consumption. Two years ago we registered the first case of poisoning after poached egg jellyfish consumption. *Case report:* We present the case of a 41-year old female who had eaten poached egg jellyfish. She was being properly treated with levothyroxine sodium because of hypothyroidism and had found information that poached egg jellyfish is rich in iodine and may be good for her disease. After her first meal with poached egg jellyfish one year before, she did not have any reaction. This time, twenty minutes after consumption of one fresh raw poached egg jellyfish she had double vision, ataxia, twitching of face muscles and cramps in the extremities and lost her balance. At admission to the General Hospital one hour after ingestion all signs were still present. Her blood pressure, heart and respiratory rate were normal. Laboratory examination including arterial blood gas analysis, white blood cells, electrolytes, blood urea nitrogen, transaminases and serum level of calcium and magnesium were normal. Activated charcoal was administered, other therapy was not necessary. In the next ten hours the symptoms gradually disappeared. Next day she was discharged without any problems. This summer we found another case with exactly the same symptoms beginning twenty minutes after consumption of poached egg jellyfish and additionally mild transitional paralytic symptoms. *Conclusion:* We did not find any other such reports after jellyfish consumption in the literature. Regarding the known data from the literature about neurotoxic seafood poisoning from filter feeding shellfish, it is also possible that contamination of jellyfish with dinoflagellates could be the reason for the described symptoms.<sup>1</sup> We have not found data that jellyfish produce such toxins. *Reference:* 1. Harris JB, Goonetilleke A. Animal poisons and the nervous system: what the neurologist needs to know. *J Neurol Neurosurg Psychiatry* 2004; 75 Suppl 3:iii40–6.

#### 46. Gila Monster Envenomation Resulting in Significant Clinical Effects

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*Objective:* The Gila monster (*Heloderma suspectum*) is a venomous lizard found in the deserts of southwestern United States and northern Mexico. Its bite is capable of causing significant clinical effects.<sup>1</sup> This case of Gila monster envenomation describes rare (angioedema, hyperesthesia) and a previously unreported clinical effect (subcutaneous air on x-ray) that necessitated operative exploration and resulted in severe, prolonged morbidity. *Case report:* A 29-year-old man was bitten on the left forearm by a wild Gila monster. The animal remained attached for ten minutes prior to being killed and removed. The patient experienced immediate, localized pain and edema followed by repeated emesis, diffuse myalgias and diaphoresis. Initial vital signs were: HR – 128, BP – 142/104, RR – 22, Temp 36.7°C. Moderate subcutaneous air was seen on x-ray of the patient's forearm. He developed progressive forearm edema and erythema with significant axillary lymph node tenderness. Twelve hours after the envenomation, the patient developed paresthesias and angioedema of the lower lip and uvula. Edema and erythema progressed into the axilla and neck; relevant blood work revealed a leukocytosis (WBC 27.3K/mm<sup>3</sup>; 4–11), and

mild coagulopathy (PT 16.2 sec; 12–15). He was taken to the operating room for surgical evaluation; there was no evidence of purulence or myonecrosis. He underwent delayed closure and split thickness skin grafting and was discharged on hospital day four. Two days later (six days post-envenomation), he was re-admitted for recurrent emesis, persistent hyperesthesia and weakness of his left upper and lower extremities. Further workup was negative; the surgical wound was not infected. Gabapentin was started with improvement. The patient was lost to follow up. *Conclusion:* In this patient, a Gila monster bite led to significant clinical effects including evidence of local inflammation, systemic envenomation and subcutaneous air suspicious for soft tissue infection. *Reference:* 1. Russell FE, Bogert CM. Gila Monster: its biology, venom and bite - a review. *Toxicon* 1981; 19:341–59.

#### 47. Marine Envenomation in Tropical Singapore

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*Objective:* Study the epidemiology of marine injuries in Singapore to identify risk factors and recommend prevention strategies. *Methods:* Retrospective, descriptive study of patients with marine injuries who presented to Changi General Hospital Emergency department from May 1999 to April 2009. Marine injuries were identified from International Classification of Diseases (ICD) code E905 and E906. Study was approved by Singhealth IRB and funded by the hospital research fund. *Results:* 394 patients were identified: 323 (82%) male, 71 (18%) female. Median age was 20–29 years old. One hundred and sixty-eight (42.5%) patients attended within 2 hours after being injured. Most injuries (88.1%) were in the extremities (hand, foot/ankle), with only 23 (5.9%) being on the trunk and face. Various sea creatures were encountered, common ones were catfish 86 (21.8%), jellyfish 44 (11.2%), stingray 36 (9.1%), stonefish/lionfish 25 (6.3%), other fish 44 (11.2%), sea urchins 6 (1.5%), sea snake 4 (1%). In 109 (27.7%) patients, the sea creature was not identified. Puncture wounds were encountered in 210 (53.2%) patients, generalised erythema and swelling in 152 (38.6%) and lacerations in 25 (6.3%). Barbs, scales or spines caused 157 (39.8%) injuries, 145 (36.8%) were bites and 76 (19.3%) patients were injured by stings. X-rays were done for 214 (54.3%) patients but only 39 (9.9%) were found to have retained foreign body in the wound. Four of the foreign bodies were found without X-rays. Three hundred and twenty (81.3%) patients required analgesia – 149 (37.8%) were given non-steroidal anti-inflammatory drugs and 89 (22.6%) were given opiates. Eleven (2.8%) patients had a regional or local nerve block done for pain relief. One hundred and ninety-one (48.5%) patients were admitted and 49 (12.4%) had surgery. There were no fatalities encountered and serious complications were uncommon. *Conclusion:* The majority of patients were young adult males. Certain behaviors at risk were identified from the patterns of injury i.e. walking along beaches, wading in shallow waters without protective footwear, careless handling of the fish caught, without appropriate gloves. Educational strategies with the aim at modification of these risk behaviors are recommended and should be targeted at high-risk groups. *Reference:* 1. Taylor DM, Ashby K, Winkel KD. An analysis of marine animal injuries presenting to emergency departments in Victoria, Australia. *Wilderness Environ Med* 2002; 13:106–12.

#### 48. Yes or No for Serotherapy in the Treatment of Scorpion Stings and Envenomations: A Systematic Review

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*Objective:* Scorpion stings are common to some parts of the world, and are a real public health problem in many countries.<sup>1</sup> Consequences can be severe, possibly producing multi-system organ-failure and death. In 2005 a synthesis of Foëx has demonstrated that intravenous administration of antivenom reduces serum venom concentrations<sup>2</sup>, but the question remained open for antivenom clinical relevance. A systematic review was carried out to assess the clinical utility of antivenom in scorpion envenomation and health outcomes. *Methods:* Search strategy: Medline 1974–10/2011 using the OVID interface. [(“scorpions”) AND (“envenomation” OR “envenomation”) AND (“antivenins” OR “antivenom” OR “immunization” OR “serotherapy” OR “immunoglobulins”) AND (Humans[Mesh] AND (English[lang] OR French[lang] OR Spanish[lang]))]. Comparators: treatment with or without scorpion antivenom. A clinical bottom line was stated. The author, date, and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of these best papers were tabulated. *Results:* While there are many case series and retrospective reviews in the literature (101 papers) suggesting that scorpion antivenom is safe and effective, there are only ten clinical trials of this treatment. Six of them showed no improvement in symptoms or in preventing symptom progression. There was no difference in hospital admission rate or duration of stay, and no difference in mortality. Only one study found any clinical improvement and this was mainly for local symptoms. Another study demonstrated that intravenous administration of scorpion-specific F(ab')<sub>2</sub> antivenom resolved the clinical syndrome within 4 hours and reduced the need for concomitant sedation with midazolam. Two studies proved that recovery from scorpion sting is hastened by simultaneous administration of scorpion antivenom plus prazosin compared with prazosin alone. *Conclusion:* There is very little evidence that giving antivenom will improve clinical outcome in scorpion stings. Multi-center trials are needed to determine the effectiveness of scorpion antivenom. *References:* 1. Elatrous S, Besbes-Ouanes L, Fekih Hassen M, et al. Severe scorpion envenomation [Article in French]. *Médecine tropicale* 2008; 68:359–66. 2. Foëx B, Wallis L. Best evidence topic report: Scorpion envenomation: Does administration of antivenom alter outcome? *Emerg Med J* 2005; 22:195.

#### 49. Scorpion Venom Induced Insulin Resistance and Inflammation in Adipose Tissue

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*Objective:* Treating mice with scorpion venom “*Androctonus Australis hector*” (Aah) results in an inflammatory process characterized by systemic cytokine production.<sup>1</sup> Here, we characterized tissue inflammation in mice following Aah injection with a focus on adipose tissue and investigated the potential role of TNF- $\alpha$ . *Methods:* We performed a kinetic envenomation protocol (0.45 mg/kg subcutaneous injection) in adult C57BL6 mice (n = 6,

aged 1 month). Inflammatory responses were performed by ELISA and cell sorting analyses in adipose tissue. Quantitative real-time PCR was used to assess the regulation of genes implicated in glucose uptake. **Results:** We showed an increase in the fed level of seric glucose (control:  $12.34 \pm 2.6$  mmol/L vs Aah:  $7 \pm 0.9$  mmol/L  $p = 0.03$ ) and insulin (control:  $1.08 \pm 0.5$  mmol/L vs Aah:  $0.34 \pm 0.08$  mmol/L  $p = 0.05$ ), 45 minutes following injection of Aah venom or its toxic fraction (FTox-G50). At later time points (24 hours), the glucose level was restored to its normal level, while hyperinsulinemia persisted. Our results indicate an increased expression of IL1 $\beta$  primarily in the sera 45 minutes following envenomation (control:  $148.66 \pm 19$  pg/mL vs Aah:  $28.3 \pm 11$  pg/mL  $p = 0.001$ ) which dropped to the basal level at 24 hours p.e. The pathophysiological effect of the venom at 24 hours was mainly characterized by M1-proinflammatory macrophage infiltration in adipose tissue accompanied with high level of IL1 $\beta$ , IL6 and TNF- $\alpha$ . Indeed, TNF- $\alpha$  was strongly induced in adipose tissue (control:  $98.20 \pm 30$  pg/mL vs Aah:  $29.11 \pm 11$  pg/mL  $p = 0.05$ ). These observations lead us to examine the effect of Aah venom on the insulin regulation of gene expression implicated in glucose uptake. Insulin induced a significant increase in hexokinase II and phosphatidylinositol 3-kinase mRNA levels in both adipose tissue and skeletal muscle of control mice. In contrast, upregulation of these genes was completely abolished in envenomed mice at 24 hours with Aah or FTox-G50. **Conclusion:** Using TNF- $\alpha$  inhibitor etanercept strongly suggest that the venom action mechanism on insulin resistance is TNF- $\alpha$ -dependent and is mediated in part by Map4k4 kinase activation in adipose tissue. Better understanding of the mechanisms involved in the adipose tissue inflammation may allow more efficient ways to prevent or attenuate the systemic and local inflammation after scorpion sting. Reference: 1. Adi-Bessalem S, Hammoudi-Triki D, Laraba-Djebari F. Pathophysiological effects of *Androctonus australis* hector scorpion venom: tissue damages and inflammatory response. *Exp Toxicol Pathol* 2008; 60:373–80.

#### 50. Autonomic Storm and Scorpion Envenomation in Children: Experience of the University Hospital of Fez

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**Objective:** Scorpion sting is a public health problem in Morocco. The most severe cases occur in children. Scorpion envenomation can be accompanied by hyperglycemia resulting from an increase in hepatic glycogenolysis inhibition of secretion and insulin action and increased secretion of glucagon. The aim of the present prospective study is to describe the endocrine manifestations of severe scorpion envenomation in children. **Methods:** We report a prospective study including children admitted in the Hassan II University Hospital in Fez for severe scorpion envenomation during two years (2009–2010). **Results:** 46 cases required medical attention. Male children constituted 80% of the cases. The mean age of the patients was  $69 \pm 46$  months. The mean time that elapsed between sting and first medical attention was 5 hours. Neurological distress (altered consciousness, coma, restlessness, convulsive crisis) was found

in 56.5% of children with severe envenomation. Cardiac failure was present in 68% and respiratory distress in 40%. The mean of glycemia values was  $26.7 \pm 19$  mmol/L (higher than 8.3 mmol/L in 20%). The glycemia was statistically associated with the neurological failure ( $p = 0.04$ ). **Conclusion:** Scorpion envenomation causes an autonomic storm releasing massive amounts of catecholamines confirming the biochemical changes and endocrine manifestations of envenomation produced by scorpion envenomation in animals.

#### 51. Severe Scorpion Envenomation in Children:

##### Experience of the University Hospital of Fez

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Severe scorpion envenomation (SSE) is a phenomenon accidentally encountered in tropical and subtropical regions. It is a real public health problem in Morocco because of its high incidence and significant lethality. **Objective:** The aim of our work is to undertake a descriptive analysis of SSE cases admitted to the pediatric and pediatric intensive care unit and to make a comparative analysis of various life-threatening aspects. **Methods:** It was a prospective study of about 46 cases of SSE in children admitted to the intensive care unit of Hassan II University Hospital of Fez during the period of 1 January 2009 to 31 December 2010. **Results:** There were 37 boys and 9 girls whose median age was 4.5 years. Clinically, the systemic signs were dominated by vomiting (65%), sweating (65%), priapism (41%), and tachycardia (33%). Cardiovascular failure was present in 67.3% of cases followed by neurological distress in 56.5% of cases. 39.3% of patients had respiratory distress. Forty per cent were class III at admission. The evolution to death was noted in 3 children. Symptomatic treatment of pulmonary oedema or cardiogenic shock (dobutamine has proven effective in the context of severe scorpion envenomation). **Conclusion:** Prevention and education are an essential part of the national strategy against the scorpions.

#### 52. A Case of Rhabdomyolysis and Axonal Neuropathy from Ingestion of “Spanish Fly” Cantharidin

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**Objective:** To report the first case of axonal neuropathy following ingestion of a blister beetle. Cantharidin, a type of terpenoid, is a toxin and vesicant secreted by many species of blister beetle, most notably the Spanish fly, *Lytta vesicatoria*. To date there are no published reports of rhabdomyolysis and/or axonal neuropathy following ingestion of cantharidin. **Case report:** A 29-year-old male residing in Malta presented to the emergency department 24 hours after voluntary ingestion of a single blister beetle. He presented in renal failure with a creatine kinase increased of 17,000 IU/L. Despite three days of haemofiltration and noradrenaline infusion, he subsequently developed disseminated intravascular coagulation (DIC), ascending neuropathy and fixed pupils. Electromyography and nerve conduc-

tion studies confirmed axonal neuropathy. We are not aware if the patient recovered from this clinical situation. **Discussion:** The toxicity of cantharidin is well documented and as little as 10 mg of the pure chemical has resulted in death.<sup>1</sup> The cantharidin content of one beetle ranges from 0.6% to greater than 5% dry weight.<sup>2</sup> The most common features reported from ingestion of cantharidin are burning of the tongue and pharynx, dysphagia, drowsiness, lethargy<sup>3</sup>, crampy abdominal pain, vomiting, diarrhoea, haematemesis, gross haematuria and dysuria<sup>2,3</sup>. Renal dysfunction is common and related to acute tubular necrosis and glomerular destruction. Priapism, DIC<sup>2</sup>, seizures and cardiac abnormalities are less common<sup>2</sup>. This is the first reported case in humans where rhabdomyolysis and axonal neuropathy have been attributed to ingestion of cantharidin although signs of neurological dysfunction have been reported in horses following ingestion of blister beetles. **Conclusion:** Treatment of patients poisoned with cantharidin should take into account its properties as a cellular toxin with ability to cause multisystem organ damage and neuropathy and also its corrosive effects on the mucosa. **References:** 1. Till JS, Majmudar BN. Cantharidin poisoning. *South Med J* 1981; 74:444–7. 2. Karras DJ, Farrell SE, Harigan RA, et al. Poisoning from “Spanish Fly”. *Am J Emerg Med* 1996; 14:478–83. 3. Mallari RQ, Saif M, Elbualy MS, et al. Ingestion of a blister beetle (Mecoidae family). *Pediatrics* 1996; 98:458–9.

#### 53. Beta-Blocker and Flecainide Overdoses Induced by *Amanita proxima* Poisoning

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**Introduction:** *Amanita proxima* is a white mushroom which causes human poisonings in Southern France with reversible renal failure and mild hepatic cytolysis. This species is classically eaten after a misidentification with the edible white *Amanita ovoidea*. The renal disturbances with reduced filtration and elimination capacities (about 20% of *Amanita proxima* poisonings need hemodialysis) can lead to pharmaceutical overdoses. **Case report:** A woman, 55 years old, with a previous history of high blood pressure and atrial fibrillation treated with flecainide and acebutolol ate for dinner unidentified white gilled mushrooms picked the day before near Montpellier. Eight hours after the toxic meal, she experienced nausea and vomiting for 24 hours. She was admitted to the emergency department on day 3 due to anuria. First biological analysis revealed acute renal failure (creatininemia 720  $\mu$ mol/L and urea blood level 22 mmol/L) and a mild hepatic cytolysis (ASAT 160/ALAT 257 UI/L) matching with a diagnosis of *Amanita proxima* poisoning. Hemodialysis was performed on day 4 when sudden cardio-circulatory collapse appeared with ventricular tachycardia (treatment: external electric shock). Afterward, asystolic cardiac arrest required external cardiac massage for 15 minutes, sodium bicarbonate 42%, glucagon, intravenous lipid 20% emulsion and large amounts of adrenaline. Extracorporeal support by extracorporeal membrane oxygenation was efficient after 60 minutes of lowflow. Clinical and electrocardiogram disturbances were attributed to flecainide and beta-blocker treatment overdoses induced by the severe acute renal failure. After several complications during intensive care monitoring (traumatic, hemorrhagic, infectious), hemodialysis was stopped 27 days

after the mushroom dinner. She was discharged without anoxic sequelae from the prolonged cardiac arrest. **Conclusion:** Mushroom picking is a widespread hobby. A lot of consumers have poor knowledge concerning edible versus toxic species. This case report highlights the increased risk of pharmaceutical overdoses when unwise patients are treated with potentially dangerous molecules like antiarrhythmic drugs.

#### 54. The Incidence of Mushroom Poisoning Correlates with Weather Conditions

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**Objective:** Mushroom picking is a popular pastime in a number of countries. The more abundantly mushrooms grow, the more individuals go to collect them, setting them at risk for mushroom poisoning through the confusion of edible with poisonous species. As mushroom growing depends largely on weather conditions, we aimed to test the hypothesis that the higher the precipitation and the temperature, the higher the incidence of mushroom poisoning. **Methods:** The calls to the national poisons centre concerning mushroom poisoning were taken as a measure for the true but unknown number of cases. The daily values for precipitation (in mm per day) and mean ambient temperature (in °C at 2 m above ground) as an average from 9 representative locations in the country for each day between January 1 and October 1 2011 were provided by MeteoSwiss (Federal Office of Meteorology and Climatology). A correlation was made between the 5-day average of the number of mushroom poisoning cases and a meteo score calculated as the product of temperature and the 5-day average of precipitations at a given day. As there is a time shift between weather conditions and the consequent mushroom abundance, we looked for the interval giving the best correlation. **Results:** During the observation period 298 cases of mushroom poisoning were recorded. The large majority of cases presented with symptoms after consumption of self-collected mushrooms. Through the year three major peaks in the incidence of mushroom poisoning occurred (mid June, early August, late September through October) with a maximum of 5.8 cases per day (5-day average). The incidence of mushroom poisoning correlated best with the weather conditions 29 days previously ( $r^2 = 0.28$ , Pearson's correlation coefficient = 0.54). **Conclusion:** There is a correlation between weather conditions and the incidence of mushroom poisoning in our country. The more rain and the higher the temperature, the more frequent is mushroom poisoning. The weather conditions preceding the poisoning cases by 29 days showed the best correlation. By observing the weather conditions, poisons information specialists in poisons centres can predict the onset of the mushroom season well in advance with fair reliability.

#### 55. Two Lethal Cases of *Amanita muscaria* Ingestion in Dogs

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**Objective:** *Amanita muscaria* (fly agaric mushroom) contains the pharmacologically active isoxazole

derivatives ibotenic acid and muscimol. They act like neurotransmitters. Ibotenic acid acts on glutamic acid receptors with an excitant action and muscimol acts on GABA receptors with a depressant action.<sup>1</sup> In the literature, to our knowledge, only one previous similar fatality among dogs has been reported.<sup>2</sup> Therefore we hereby present two additional cases. **Case series:** Dog 1. Cocker spaniel, 4 months old, 8–9 kg, was out alone in the yard. Two hours later the dog became anxious, disorientated, with frothing at the mouth. Vomiting was produced and large amounts of fly agaric were seen in the vomitus. Then the dog became calm and fell asleep. The dog became unconscious 7.5 hours after the ingestion and died on the way to the veterinary clinic. Dog 2. Chihuahua, 1.5 years old male, 2.3 kg, ate an unknown amount of fly agaric. The dog vomited after 10 minutes and some mushroom parts were seen in the vomitus. Charcoal was given. Symptoms started 45 minutes later, with ataxia, seizures and breathing difficulties with wheezing. The dog was treated symptomatically with diazepam IV, oxygen, fluid IV and cortisone. X-ray showed pulmonary oedema. The condition worsened with cyanotic mucous membranes, very forced breathing and no pain reaction. As breathing and heart frequencies slowed down the dog was euthanized approximately 4 hours after the ingestion. **Conclusion:** It is unusual that ingestion of *A. muscaria* mushroom results in lethal intoxication. Normally these poisonings can be treated symptomatically with good results. **References:** 1. Michelot D, Melendez-Howell LM. *Amanita muscaria*: chemistry, biology, toxicology and ethnomycology. Mycol Res 2003; 107:131–46. 2. Spoerke D. Mushrooms. In: Peterson ME, Talcott PA, eds. Small animal toxicology. 2nd ed. St. Louis, USA: Elsevier Saunders, 2006:860–87.

#### 56. Circuitous Diagnosis in Concealed Self-Poisoning with *Nerium oleander*

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**Objective:** We report a case of deliberate self-poisoning by *Nerium oleander*, whose toxicity is related to the cardiac glycosides contained in all parts of this plant, including the sap, whether fresh, dried or boiled. Plant poisoning is globally an uncommon cause of death in adults, and is more often seen in children who unintentionally ingest small quantities of toxic plants. **Case report:** A prisoner aged 60 years, with a known depressive syndrome, presented malaise with hypotension, sweating and nausea on exertion. Myocardial infarction was suspected. The patient was admitted to a university hospital. Shortly after admission, he presented neurological and cardiac distress. Toxicological analysis revealed digoxin within the therapeutic range, a surprising finding as this substance was not prescribed for the patient. He was successfully treated with anti-digoxin Fab fragments. **Conclusion:** Because the physicians were unaware of the consumption of *N. oleander* leaves before the episode of distress, it was not possible to establish the diagnosis. Following their reasoning of digoxin poisoning, the treatment initiated was in accordance with expert opinion and consisted of the administration of equimolar doses of anti-digoxin Fab fragments at a dose of 160 mg in intravenous infusion for 20 minutes. This treatment led to an improvement in the patient's condition. Diagnosis is difficult in

view of the rarity of *N. oleander* poisoning in France. The toxic agent was in fact found to be growing in the prison garden. A careful and detailed history can facilitate the diagnosis of such poisoning.

#### 57. Aconitine Poisoning Following the Ingestion of Chinese Herbal Medicines: The Need for Promoting Awareness

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**Objective:** *Aconitum* species have been used in Traditional Chinese Medicine (TCM) for many years. The toxicity of *Aconitum* mainly derives from the diester diterpene alkaloids including aconitine, mesaconitine and hypaconitine. In Taiwan, aconite roots are used only after processing to reduce the toxic alkaloid content, however intoxications still occur. We report our experience of aconitine poisoning. **Methods:** A retrospective study was conducted to evaluate patients with suspected adverse effects from aconitum herb reported to the Taiwan Poison Control Center over a four year period from 2008 to 2011. **Results:** There were 8 men and 2 women, aged 16 to 80 years. They were identified with features of moderate to severe intoxication including nausea and vomiting, paraesthesiae or numbness in the mouth and extremities, dizziness, blurred vision, chest discomfort, palpitation, generalized weakness, ataxia, syncope, bradycardia, hypotension and ventricular dysrhythmias. Four cases ingested aconitine as treatment for pain, three cases for heart disease, one case for liver protection, one case for growth promotion and one for promotion of digestive function. All patients developed toxicity even though they took processed herb. The most commonly used herbal products containing *Aconitum* were "Fuzi" in 8 cases. The diagnosis was initially unknown in 3 cases, but was established later by aconitine quantification in patient's urine or herbal samples. **Conclusion:** Although the risk is higher with inadequately processed roots or large doses, aconitine poisoning can occur after the consumption of aconitum herbs even in therapeutic doses. With increasing popularity of TCM, the unpredictable risk of taking aconitum herbs should be alerted to the physicians and public to increase awareness. The laboratory analyses of aconitum alkaloids are also important for unrecognized cases of aconitine poisoning.

#### 58. Toxic Holiday Plant Ingestions... Or Are They?

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**Objective:** Poinsettias (*Euphorbia pulcherrima*), holly (*Ilex opaca*) and mistletoe (*Phoradendron flavescens*) adorn homes during the holiday season and create the potential for curious children to sample their colorful leaves and enticing berries. The plants are often maligned in the lay press and even in the medical literature; but are they poisonous or merely an attractive nuisance? The objective of this project was to review the American Association of Poison Control Centers National Poison Data System (AAPCC NPDS) to determine whether there was morbidity and mortality associated with the ingestion

of these plants. **Methods:** All plant ingestion exposures that were reported to American poison centers from 2000–2009 were provided to the investigators as an AAPCC data grant and analyzed using Microsoft Office Excel to identify all exposures to *Euphorbia pulcherrima*, *Ilex opaca* and *Phoradendron flavescens*. The data analysis included ingestions by age, gender, patient management site, symptoms, reason and outcome. Descriptive statistics were used to characterize the data. **Results:** The AAPCC NPDS database included 668,111 plant ingestion exposures. *Euphorbia pulcherrima* (19,862 – 3.0%), *Ilex opaca* (5,432 – 0.8%) and *Phoradendron flavescens* (1,138 – 0.2%) exposures accounted for 26,632 (4.0%) of all plant ingestion exposures. Ingestions by children less than six years of age were responsible for 87.7%, 92.6% and 73.8%, respectively, of the ingestions. When the outcome was known, 88.2% of *Euphorbia pulcherrima*, 92.0% of *Ilex opaca* and 87.5% of *Phoradendron flavescens* exposures experienced no adverse effects. Minor effects occurred in 11.3%, 7.4% and 11.9%, respectively. Moderate effect outcomes occurred in only 30 of the ingestions and one major effect was recorded in the *Euphorbia pulcherrima* ingestion patients. When symptoms developed, the most frequent symptoms were gastrointestinal in nature and most commonly abdominal pain or vomiting. Home management without health care facility referral was documented in 89.0 – 96.9% of the ingestions. **Conclusion:** These holiday plants were associated with extremely low morbidity and there were no fatalities related to these ingestions. Home management is adequate intervention in the majority of these exposures.

### 59. Severe Colchicine Intoxication with Development of Pneumatosis Intestinalis

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**Objective:** Severe colchicine overdoses may lead to multiorgan failure. Due to the lack of an available specific antidotal treatment, therapy is restricted to multimodal intensive care management. Development of paralytic ileus requiring surgical intervention is described here. **Case report:** A 70-year old female was admitted to an external hospital with prolonged diarrhoea, vomiting and abdominal pain after consumption of self-collected wild garlic prepared as a soup two days before. Laboratory analyses showed thrombocytopenia, impaired renal function, elevated liver enzymes and hypocalcaemia. Abdominal ultrasound revealed progressively dilated intestine. Intoxication with *Colchicum autumnale* was suspected, and the patient was transferred to our intensive care unit (ICU). During of the next day she developed multiorgan failure with increasing inflammation parameters, acute renal and liver failure, suppression of bone marrow and toxic cardiomyopathy subsequently requiring mechanical ventilation and vasopressors. Further treatment included antibiotics, administration of blood components and granulocyte colony-stimulating factors. Acute renal failure required transient haemodialysis. Particularly high colchicine serum concentrations were observed (4, 5 and 0.8 µg/l at day 3, 4 and 15, respectively). On the fifth day after ingestion she developed complete paralytic ileus. Computer tomography showed massive dilated intestinal loops with pneumatosis intestinalis and excessive gas accumulation in the portal vein. Due to imminent perforation a double-lumen ileostomy was necessary,

which could be performed not earlier than day 7 due to hemodynamic instability before. A postoperative CT-scan showed no further signs of pneumatosis intestinalis. In the course of the next few days organ dysfunction recovered. Because of colchicine-induced axonal neuropathy and myopathy with weakness of respiratory muscles, the patient was tracheotomised. After 30 days of hospitalisation she was transferred for further neurological rehabilitation. **Conclusion:** This case illustrates that colchicine-induced paralytic ileus may lead to fatal intestinal necrosis with the need for surgical care. To the best of our knowledge, this is the first case of severe colchicine overdose presenting with pneumatosis intestinalis. This case again emphasizes the necessity for a specific therapy, which is, despite the principal existence of colchicine-specific antibodies<sup>1</sup>, not yet available. **Reference:** 1. Baud FJ, Sabouraud A, Vicaut E, et al. Brief report: treatment of severe colchicine overdose with colchicine-specific Fab fragments. *N Engl J Med* 1995; 332:642–5.

### 60. Do Not Trust Friends: An Unusual Herbal Intoxication

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**Objective:** *Aconitum napellus* is a herbaceous plant found throughout the mountains of Central Europe and Italy. The whole of the plant, especially the roots, contains different highly toxic alkaloids, mainly aconitine. Often ingestion of the plant is accidental, due to its similarity to wild asparagus and turnips. **Case report:** Two patients, wife and husband come to the Emergency Department suffering from severe abdominal pain with vomiting, dysphagia and paresthesiae localized to face and arms. They had eaten, about 30 minutes before the symptoms appeared, a huge meal of risotto with mushrooms and herbs, picked in the nearby mountains by a relative who presented them as an “absolute rarity”. During the examination both presented with hypotension, bradypnea and tachycardia; the husband’s ECG showed monomorphic ventricular tachycardia, while the wife’s an atrial fibrillation. **Results:** The patients were treated with intensive monitoring of the vital parameters, nasogastric tube, respiratory and rehydrating supportive care. Both the arrhythmias were treated with continuous infusion of amiodarone. At the first presentation the clinical and anamnestic element led to mushroom poisoning and to confirm this hypothesis urinary amanitin was performed, with negative result. Chemical and toxicological exams were all negative, except for slight hypokalaemia in the woman. Meanwhile, the man suffered from seizures requiring high dosage sedation; his wife, after developing dysarthria and dysphagia, developed xerostomia, tremors, diplopia and altered vision to green and yellow. With a more accurate history, it emerged that the mountain herbs were similar to wild asparagus. This information combined with clinical signs and symptoms, led to a test for aconitine, which resulted positive. **Conclusion:** The case report presented shows that history is also a fundamental part of the work in the Emergency Department; in this case the keystone for making the diagnosis was the asparagus’s resemblance to aconitum. At the very beginning, the diagnostic hypotheses were addressed to mushroom poisoning, but symptoms didn’t match with times and presentation modality; persevering with this hypothesis would have led to inadequate treatment.

### 61. A Fatal Case of Suicidal Injection and Ingestion of Self-Extracted Ricin

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**Objective:** Ricin is a potent toxin listed as a schedule-1 substance in the Chemical Weapon Convention. Recent events have reinforced its potency in terrorism. Oral ingestion is well described, less is known about intravenous injection. We present such a case where the Norwegian NBC-center (nuclear, biological, chemical) was involved. **Case report:** A 21 year old man self-extracted ricin from castor beans bought on the Internet, and ingested and injected it with a suicidal intent. On admission four hours later, he was awake, circulatory and respiratory stable, with a visible puncture site in the left arm. He had signs of hypovolemia with hemoglobin 17.2 g/dL and albumin 52 g/L. One hour later he vomited, had diarrhea, progressive generalized pain, tachycardia (112/min) and respiratory rate of 30/min. Chest radiograph showed bilateral infiltrates. After 20 hours, he had a mild metabolic acidosis and evolving coagulopathy, only transiently responding to intensive care unit (ICU) treatment. At 27 hours he was hardly responding to questions, had respiratory distress with progressive bilateral infiltrates, severe lactacidosis and signs of hypoperfusion despite aggressive fluid treatment and vasopressors. Laboratory results showed liver failure. He received continuous dialysis at 31 hours, and was intubated 22 hours post exposure. He died after 42 hours in a state resembling septic shock with refractory multi organ failure. Later analyses confirmed ricin as the toxic agent. There was great concern about the toxicity of ricin to the local environment (house, neighbor) and hospital staff handling the patient and biological samples. In addition to giving advice on treatment, the Norwegian NBC-center was involved in a large variety of issues regarding the handling of biologic samples, corpus, cremation, the police seizures and coordination of sample analysis. **Conclusion:** Injected ricin caused a septic-like clinical picture with early signs of hypovolaemia, and later multi organ failure, but with scarce clinical signs the first hours. Aggressive fluid treatment should be initiated early based on laboratory findings indicating hypovolaemia. Available knowledge about the handling of all aspects of such cases is needed on a national level in these hopefully rare events. The fear of toxicity in the local environment – including health care personnel – should not be underestimated.

### 62. Surviving a Castor Bean Ingestion: Potential Protein Denaturation of Ricin and its Exposure Biomarker Ricinine

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**Objective:** To describe unprecedented urinary ricinine concentrations in a patient who exhibited only minor toxicity after castor bean ingestion. **Case report:** A 55-year-old firefighter became suicidal as the 10th anniversary of the September 11th terrorist attack approached. Using ricin, a toxalbumin derived from the castor bean plant, *Ricinus communis*, he crushed

20–30 castor beans into a fine powder, sprinkled over oatmeal, then heated in a microwave. Approximately 20% was consumed; nausea developed at the hospital where he was rapidly decontaminated with charcoal and polyethylene glycol bowel irrigation and treated with ondansetron plus supportive care. The patient was medically cleared following 72 hours of clinical stability. While ricin's bioavailability after oral ingestion is three times less toxic than inhalation/parenteral routes, some toxicity was expected given the beans had been crushed.<sup>1</sup> Using liquid chromatography/mass spectrometry, the Centers for Disease Control's analysis found, at hour 17.5 status post ingestion, peak urinary ricinine concentration of 8,540 micrograms/milliliter (17,941 micrograms per gram creatinine), the highest ever reported by this lab and on PubMed search. Ricinine, an alkaloid also extracted from the castor bean plant, is used as a surrogate marker for ricin exposure; it is a CNS stimulatory compound which can produce seizures, hyperactivity, and respiratory arrest in animal models<sup>2</sup>. Although ricinine is thought to be heat stable<sup>3</sup>, microwave radiation may result in protein denaturation. **Conclusion:** Our patient's ricinine concentration is the highest ever reported in the literature. While ricinine can be used as a surrogate for exposure<sup>4</sup>, the goal is to find a biomarker that can be utilized for clinical correlation to the toxin ingested. Because ricinine appears to be inactivated by microwave radiation, it may have limitations in this setting. **References:** 1. Bradberry S, Dickers K, Rice P, et al. Ricin poisoning. *Toxicol Rev* 2003; 22:65–7. 2. Audi J, Belson M, Patel M, et al. Ricin poisoning. *JAMA* 2005; 294:2342–51. 3. Johnson R, Lemire S, Woolfitt A, et al. Quantification of ricinine in rat and human urine. *J Anal Toxicol* 2005; 29:149–55. 4. Musshoff F, Madea B. Ricin poisoning and forensic toxicology. *Drug Test Anal* 2009; 1:184–91.

### 63. Plant Poisoning in Thailand: A 10-year Analysis from Ramathibodi Poison Center

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**Objective:** Epidemiological data of plant poisoning in Thailand are scarce. This study represents the primary data regarding plant exposures of the country. The objective is to characterize type of toxic plants, incidence of poison exposures and severity of plant poisoning in Thailand over 10 years. Humans frequently have contact with plants, some of which are toxic. **Methods:** We carried out a retrospective study by reviewing plant exposure cases from the Ramathibodi Toxic Exposure Surveillance database during 2001–2010. Toxic plants, patients, clinical manifestation and clinical outcome were analyzed. **Results:** Of 92,392 cases we have collected, plant exposures ranked the fifth most common poisoning in Thailand with 2,901 cases. The median age of patients was 9 years old (2 months to 93 years old) with the highest incidence in children less than 12 (69.8%). Male-to-female ratio was 1.5:1. Unintentional exposure constituted the majority of poisoning and oral ingestion was the main route of exposure. Physic nut (*Jatropha curcas*) was the most common poisonous plant accounting for 53.8%, followed by wild yam (*Dioscorea hispida*, 8.7%), cassava (*Manihot esculenta*, 6%) and Jimson weed (*Datura spp.*, 4.1%). Gastrointestinal symptoms were the most prominent clinical manifestations in nearly all poisonings. Ninety-four per cent of patients had no or mild symptoms at the time when consultations were

made. For the final outcome, the majority had minor effects, only 1.1% developed major effects and 0.9% died. Exposures to physic nut represented the highest cause of plant poisoning but only minor effects were developed with no mortality. The common plants causing fatalities were cassava, rosary bean (*Abrus precatorius*), glory lily (*Gloriosa superba*) and wild yam. Of all 26 fatal cases, 14 cases were children aged 2 to 8 years. **Conclusion:** Poisoning from plants in Thailand was mostly unintentional, rarely responsible for severe poisoning and had a low mortality rate. The most common culprit plant was physic nut, but the leading cause of death was cassava. Young children were the susceptible group for toxic plant exposure and poisoning. Public education is essential to decrease the incidence and prevent intoxications effectively.

### 64. A Survey of Athletes and their Use of Performance Enhancing Substances

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**Objective:** Athletes feel significant pressure to succeed and win. As a group, they utilize various substances to enhance their performance. Among these, we hypothesize that energy drink, dietary supplement, and prescription medication use is highly prevalent among United States (US) college athletes. Currently, many of these products are not banned by the National Collegiate Athletic Association (NCAA). Aside from the obvious dangers of some prescription medications, energy drinks and dietary supplements are largely unregulated and contain ingredients that can pose potential health hazards. The purpose of this survey is to analyze the rate of energy drink, dietary supplement, and prescription medication use in US college athletes for performance enhancement. **Methods:** The RADARS® System College Survey Program is a multi-round online questionnaire collecting data from self-identified students who are enrolled in two-year colleges, four-year colleges, online courses, or technical schools at least part-time during the specified sampling period. Respondents complete an online questionnaire. The subjects are asked if they participate in athletics, at what level, and if they have taken an energy drink, dietary supplement, or prescription medication within the last year in order to enhance their athletic performance. **Results:** 462 college students responded to the survey reporting they participate in sports at various levels. Of these, 397 (85.9%) used energy drinks, dietary supplements, or prescription medications before or after their particular athletic event within the last year. Across different sport levels, use of performance enhancing agents was most prevalent amongst intercollegiate athletes (89.4%). Among the different performance enhancing substances, energy drinks had the highest prevalence (80.1%). **Conclusion:** The vast majority of those surveyed in our study reported using energy drinks, dietary supplements, and prescription medications within the last year for performance enhancement. Energy drinks were the most prevalent of the three groups of substances. Likely, the high prevalence of energy drink usage is directly related to their ubiquitous availability and a perceived relative short term physiologic effect. More concerning is the high prevalence of prescription medication usage. Limitations of the survey are that the data collected is reliant upon the accurate responses of those surveyed and all respondents take the survey voluntarily.

### 65. Hapalopilus rutilans Poisoning: Report of Two Cases

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**Objective:** Only three cases of *Hapalopilus rutilans* poisoning have been previously published.<sup>1</sup> We report two new cases. **Case report:** A father and his 13-year-old daughter picked mushrooms identified as *Fistulina hepatica* specimens and cooked and ate an unknown amount (H0). At H12, both subjects complained of abdominal pain, followed by nausea, vomiting, anorexia, asthenia, diplopia, blurred vision; the father also reported visual hallucinations. On D2, clinical examination showed multidirectional nystagmus. The father also presented balance disorders and both subjects reported purple urine. Laboratory test results showed elevation of plasma creatinine, proteinuria and leukocyturia in both subjects and slight elevation of hepatic enzymes in the father only. Urine colour returned to normal on D2 in the daughter and D7 in the father; complete clinical and laboratory recovery was obtained within 8 days in both cases. **Conclusion:** This clinical presentation is similar to the symptoms and signs previously reported after *Hapalopilus rutilans* ingestion; this mushroom can be confused with *F. hepatica*<sup>1</sup> and the father recognized *H. rutilans* from pictures. Purple discoloration of urine after ingestion of a polypore mushroom is highly suggestive of *H. rutilans* poisoning. The active toxin is probably polyporic acid (PA), which has been found in *H. rutilans*. Administration of PA to rats reproduced the signs of human poisoning.<sup>1</sup> **Reference:** 1. Kraft J, Bauer S, Keilhoff G, et al. Biological effects of the dihydroorotate dehydrogenase inhibitor polyporic acid, a toxic constituent of the mushroom *Hapalopilus rutilans*, in rats and humans. *Arch Toxicol* 1998; 72:711–21.

### 66. Jatropha curcas Poisoning, Report of 13 Cases

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**Objective:** *Jatropha curcas* is an inedible plant belonging to the *Euphorbiaceae* family and growing in subtropical zones of all continents. We report a series of 13 cases of poisoning with *J. curcas* seeds notified to the Paris poison and toxicovigilance centre between December 2000 and June 2011. **Case series:** 12 adults (17–41 yrs, 9 men and 3 women), and one girl (9 yrs) ate 2 to 15 *J. curcas* seeds (median: 10). All patients experienced gastrointestinal disorders, one to 3 hours after ingestion: nausea, vomiting (13 cases), diarrhoea (10 cases), and abdominal pain (8 cases). Laboratory investigations performed in 10 patients revealed minor abnormalities: CPK elevation (1.1 and 3.9 N; 8 cases), dehydration (5 cases) with serum creatinine levels of 109–131 µmol/L (3 cases). All clinical signs resolved within 48 hours in the 12 cases for which the outcome was known. Serum electrolytes and creatinine levels returned to normal within 24–48 hours; CPK levels were not monitored. **Conclusion:** More than 70 cases of *J. Curcas* poisoning after seed ingestion have been previously published. Most cases

occurred in warm, developing countries. As in our series, gastrointestinal disorders were always present and were sometimes associated with neurological or cardiovascular signs, and hepatic or renal disorders, which can always be interpreted as complications of severe gastroenteritis, although direct toxic effects cannot be formally excluded. Severe gastrointestinal disorders after ingestion of *J. curcas* seeds require monitoring of fluid and electrolyte balance, serum creatinine, CPK and hepatic enzymes. In most cases, simple supportive measures are sufficient to ensure complete recovery within 24–48 hours.

### 67. Arsenic Contamination of Groundwater in West Bengal, India: A Continuing Public Health Hazard and Issues in Mitigation: Perspectives from the Field

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**Objectives:** A one month placement at the Debendra Nath Guha Mazumder Research Foundation (DNGMRF) in Kolkata, West Bengal formed part of a year long programme of sub-specialty training in clinical toxicology at the Health Protection Agency. The aims of this placement were to understand the nature and magnitude of the health effects caused by arsenic, the historical evolution of the hazard, types of interventions put in place to mitigate against arsenic and issues faced in preventing ongoing exposure. **Methods:** A background literature review was carried out in order to understand the evolution of arsenic as an environmental hazard in the region and the pathways through which the population was being exposed. This was supplemented by review of a limited number of government policy and planning documents held in the library of the DNGMRF, field visits to three affected villages and semi-formal interviews with field workers and villagers. **Results:** In 2000, the scale of the public health impact of arsenic contaminated drinking water in Bangladesh and the neighbouring Indian state of West Bengal was first brought to light.<sup>1</sup> The World Health Organisation described it as the largest mass poisoning of a population in history.<sup>2</sup> The exposure was brought about inadvertently as a result of the siting, during the 1980s and 1990s, of millions of tube-wells for the extraction of groundwater, which being far superior to surface water in terms of microbial contamination was considered a 'safe' drinking water source. However the aquifers turned out to be contaminated with arsenic. Observations made during fieldwork as well as through interviews highlighted some of the difficulties faced in the ongoing mitigation efforts. These include factors such as the remote locations of many of the affected villages; the chronic cumulative nature of the toxic insult which often makes arsenic a low-priority issue for villagers with more pressing health and livelihood concerns; and the multiple pathways by which exposure might occur e.g. drinking water and dietary sources. **Conclusions:** An unfortunate and unintended consequence of extracting groundwater on account of microbial safety, inadequate testing for chemical contaminants has led to a public health catastrophe across Bangladesh and West Bengal that continues to cause ill-health and pose challenges for mitigation today. **References:** 1. Chowdhury UK, Biswas BK, Chowdhury TR, et al. Groundwater Arsenic Contamination in Bangladesh and West Bengal, India. *Environ Health Perspect* 2000; 108:393–7. Available at <http://dx.doi.org/10.1289/ehp.00108393> [accessed 17/12/2011]. 2. World Health

Organisation 2002 Arsenic – Mass poisoning on an unprecedented scale. Available at <https://apps.who.int/inf-fs/en/feature206.html> [accessed 09/12/2011]

### 68. Environmental Testing for Lead in Accra, Ghana

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**Objective:** Lead is an established environmental toxin and the most common metal responsible for poisoning. Through the combination of environmental regulation and whole population screening, the incidence of lead poisoning has been greatly reduced in many countries world-wide. Similar approaches are now being adopted in West African countries like Ghana, which banned the sale of leaded gasoline in 2003. However such regulations are far from institutionalized and many adults and children remain at risk. **Methods:** This research was undertaken as a first step to identify common environmental sources of lead in Accra, Ghana, with the goal of developing testing and risk reduction strategies. Samples of soil, pottery, paint, and other objects from thoroughfares, playgrounds, markets, and gas stations were collected. Samples were taken from areas easily accessed by passersby, including children, in a convenience sample of neighborhoods suspected of being at greatest risk of lead exposure. Coordinates for each sample were determined using a handheld Global Position Satellite device and were marked on a standard map. Each sample was tested in an identical manner using Lab Inspector Lead Test Kits from Abotex, which uses a sulfur-based solution to produce a semiquantitative color change in the presence of lead. **Results:** Out of a total of 332 samples, there were 75 positive **Results:** 33 soil, 10 eating utensils, 14 building tiles that had fallen onto the road, 5 cans that had previously contained foodstuffs, 2 bowls with chipped paint, 5 pieces of metal jewelry, 2 paint chips scraped from walls, 2 pieces of solder/wire, one discarded battery, and one sample of liquid herbal medicine. Thirteen of the positive soil samples were taken from the sites of gasoline retailers. The majority of the positive samples were collected in less-developed residential neighborhoods and lower socioeconomic areas. **Conclusion:** The data presented above indicates that lead is likely present in the environment in Accra, Ghana, and exposure to the population is a concern. We advocate consideration of lead exposure in both individual and population-based environmental health risk assessments, and hope to begin widespread testing in areas where risks of exposure seem highest.

### 69. Stockpile of Antidotes for Radiological Incidents

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**Introduction:** The Dutch Poisons Centre (PC) has a team of radiation experts who advise on the medical treatment of casualties after incidents with radioactive material and/or ionizing radiation. After realizing a stockpile for stable iodine tablets (to block uptake

of radioactive iodine in the thyroid gland after exposure), it was recognized that antidotes to treat internal contamination with other radionuclides are not readily available in the Netherlands. Following internal contamination, administration of a specific antidote capable of binding the radionuclide is important because radionuclide elimination is increased and consequently radiation dose reduced. This treatment is most useful directly after exposure. **Discussion:** When looking at indications and effectiveness, Prussian Blue (for cesium and thallium) and diethylenetriaminepentaacetate (DTPA) (for cesium, americium, curium, californium and plutonium etc) are the most useful antidotes. They cover a wide range of radionuclides, including those most likely to be used in a dirty bomb (that spreads radionuclides on detonation). For DTPA, the calcium salt (Ca-DTPA) is most effective in the early phase after exposure, while the zinc salt (Zn-DTPA) is recommended for prolonged treatment. A stockpile of these three antidotes ensures early administration. A stockpile to minimally treat 50 persons during the first 10 days after exposure seems sensible (treating more people for a shorter period is possible; e.g. 100 persons for 5 days). This amount is based on a well-known, large incident with a dismantled radioactive cesium source in Goiânia. The purchase costs of these antidotes are estimated at around 3500 euro/year (in 2011), taking into account the 5 year shelf life. This is low related to the benefit such a stockpile can provide. If prolonged treatment is necessary, new antidotes can be purchased from a pharmaceutical company. For Prussian Blue, for example, the reported delivery time is minimally two working days. **Conclusion:** For the direct medical treatment of persons internally contaminated with radionuclides, it is advisable that every country has a stockpile of suitable antidotes. The Dutch PC advised the Ministry of Health to establish, besides the already available stable iodine, an antidote stockpile with Prussian Blue, Ca-DTPA and Zn-DTPA. The proposal awaits formal acceptance.

### 70. Prevalence and Determinants of Depression Tendency in a Prolonged Low-Dose Rate Radiation Exposed Cohort in Taiwan

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**Objective:** More than 7,000 people were found to be exposed to low-dose-rate gamma radiation contaminated buildings in Taiwan in 1992. Among these, long-term stress originating from the fear of radiation exposure related adverse health effects had been observed in some subjects; however no study had been conducted to evaluate the risk of developing depression in this special cohort [also known as "Radiation Contaminated Building (RCB)" cohort]. **Methods:** We conducted an interviewer-assisted questionnaire survey among 2,143 subjects who received an annual physical checkup at a pre-specified hospital between March and December 2009. A total of 1,707 subjects who fulfilled the inclusion criteria agreed to participate in the study and filled out a questionnaire that included personal information, Beck Depression Inventory (BDI)-II Scale and Depression and Somatic Symptoms Scale (DSSS). All data were then analyzed

by employing multivariate logistic regression analyses to identify potential predictors of depression tendency (i.e. BDI > = 14). **Results:** We found that the prevalence of depression tendency was 14.5% among all study subjects (17.6% among subjects with relatively high dose exposure (excess dose > 5 mSv); and 13.5% among subjects with relatively low dose exposure group (excess dose = 1–5 mSv). Moreover, education level was inversely associated with depression tendency (OR 0.63, 95% CI 0.49–0.80). Individuals who worried more about the potential adverse health effects of radiation exposure and who had more somatic symptoms were more likely to have depression tendency (OR 1.65, 95% CI 1.41–1.94 and OR 1.35, 95% CI 1.23–1.48, respectively). **Conclusion:** The prevalence of depression tendency in the RCB cohort was 14.5%. Less educated people, those who worried more about the potential adverse health effects of radiation exposure and those with more somatic symptoms were more likely to have depression tendency. The study findings suggested that past radiation exposure experience might lead to long-term psychological stress and subsequent depression tendency.

### 71. Pattern of Drug and Chemical Poisoning in Sari City, Northern Iran, Over One Year

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**Objective:** The aim of this study was to characterise patients presenting to a poisoning referral hospital following drug and chemical overdose. **Methods:** This cross-sectional retrospective study was performed over a one-year period from April 2008 to March 2009 and included all patients referred to Imam Teaching Hospital, a referral hospital for drug and chemical poisoning, in the city of Sari, northern Iran. Data including demographic characteristics, types of poisoning, amount ingested, intention of overdose, history of suicide, first signs and symptoms of overdose, length of hospitalization and outcome. Collected anonymous data were analyzed using descriptive statistics. **Results:** Over a one-year period 729 patients were admitted to the hospital following overdose. Most patients were female (54.2%) and young adults of 20–30 years of age (49%). The main intention of the overdose was suicidal (93%). The majority of patients lived in urban areas (81.3%). The most common cause of suicide was family issues (53.2%), followed by relationship (24.1%) and financial (15.7%) problems. Among drugs, tramadol (20.7%) and benzodiazepines (15.2%) and among chemicals, aluminum phosphide poisoning (7.7%) known as “Rice Tablet” were the most common agents involved in overdose. 66.6% of patients presented to the hospital within an hour post ingestion. Length of hospitalization was 2 days or less in more than 75% of patients. Eighteen patients (3%) died. Aluminum phosphide poisoning was the most serious type of toxicity leading to 7 deaths. **Conclusion:** Poisoning is a common health problem in Mazandaran province. Most cases of poisoning occurred in the young-adult, in particular with suicidal intention. Opiate analgesics followed by benzodiazepines were the most common agents associated with poisoning. Aluminum phosphide toxicity was the most serious toxicity leading to death.

### 72. Elderly People and Poisoning: Epidemiology of Poisoning in the New Zealand Population

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**Objective:** To characterize the pattern of poisoning in the elderly New Zealand Population. **Methods:** A 5 year retrospective study was conducted of telephone enquiries to the National Poisons Centre from January 2006 to December 2010 inclusive. All exposure cases concerning patients aged over 65 years were identified. Information on patient age, sex, type of agent(s), and location, route, and other circumstances of exposure was collated. Patients were grouped according to age (65–69, 70–74, 75–79, 80–84, 85–89, 90–94, 95–99, > 100 years). **Results:** During this 5 year period the centre received 2,296 actual exposure calls, (650 calls involving more than one substance). Patient age ranged from 65–102 years and poisoning was most prevalent in the 65–69 years age group. Females predominated in all age groups, with the overall female-to-male ratio being 1.8 to 1. About 51.7% of exposures involved medicines, 25.3% household products, 8.0% agricultural products and the remainder included industrial agents, cosmetics, bites/stings and plants. Cardiovascular medicines, analgesics, antidepressants, hypnotic/sedatives and psycholeptic agents were the predominant pharmaceuticals involved, while the main chemicals included bleach, detergent, pesticides/herbicides, surfactants/cleaners and denture cleansing products. Ingestions accounted for 73.3% of all exposures. A total of 1,418 cases (61.8%) required either no treatment or only self management, whilst 843 cases (36.7%) were referred for medical assessment, observation or active treatment and 35 (1.5%) were recorded as further information required. There were 61 cases of intentional ingestions. Notably, 80% of these calls involved only a single substance, some at toxicologically significant doses. **Conclusion:** Forgetfulness, incorrect use of the product or simply mistaking one product for another was commonly cited in these calls as the cause of the exposure. In order to reduce toxic exposures in elderly patients, an in depth analysis of the circumstances behind these poisonings needs to be undertaken to assist with developing poison prevention strategies emphasizing chemical safety, appropriate use of pharmaceuticals, and regular review of prescribed medicines.

### 73. Acute Clonazepam Poisonings in Slovakia: A Ten Year Review

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**Objective:** Poisonings involving clonazepam are among the more common inquiries to the National Toxicological Information Centre (NTIC) in Bratislava. To evaluate the safety profile of clonazepam in overdose, we performed a retrospective analysis of all intoxications by clonazepam about which the Slovak NTIC were consulted during the ten year period. **Methods:** Intoxications were analyzed on the basis of data gathered from telephone consultations and medical reports forwarded to the NTIC in Bratislava from the whole area of Slovakia in the years 2001–2010. **Results:** During the study period the NTIC was consulted about 1508 antiepileptic intoxications, of which 431 involved clonazepam. Fifty-seven per cent of

all patients were female, 42% were male. The highest numbers (123) were in the age ranges 19–35 years and 36–50 years (117); most of these cases were suicidal attempts. Accidental poisoning was most common in children under 5 years of age and those aged over 65 years. Sixty-one per cent of intoxications were mixed, particularly with alcohol and antidepressant, anxiolytic and antiepileptic drugs. The most common poisoning severity score (68% cases) was PSS 1, which means intoxications accompanied by mild, transient and spontaneously resolving symptoms – fatigue, somnolence, ataxia. There were five lethal cases as a consequence of mixed drug intoxications with suicidal intent. In most cases, hospital treatment was non-specific decontamination and supportive/symptomatic therapy. Ninety-seven patients received activated charcoal, 55 activated charcoal with laxative, 38 gastric lavage and 12 patients were given the specific antidote flumazenil. **Conclusion:** Clonazepam overdose is associated with relatively low morbidity and mortality. Most deaths associated with clonazepam result from mixed overdoses with other central nervous system depressants, especially alcohol. We found an increasing tendency in clonazepam intoxications, which were mainly due to suicide attempts. In spite of the fact that it is mandatory to report intoxications to the NTIC, there are still medical facilities which do not fulfil this requirement. If all the medical reports were available, there would be a greater possibility to introduce measures to lower the number and consequences of intoxication.

### 74. International Perspective of Prescription Stimulant Exposures Reported to Poison Centres from 2007–2010

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**Objective:** Prescription stimulant abuse is on the rise in the United States (US). Abuse in other countries is not well studied. The objective of this study is to characterize human exposures to specific prescription stimulants reported to poison centres from multiple countries over a four year study period. **Methods:** Human exposures to methylphenidate and amfetamines reported to poison centres from 2007–2010 were obtained using a standardized data template with written definitions. Rates are reported as number of exposures reported to poison centre per 100,000 population. **Results:** Seven countries participated; Australia, Germany (Göttingen), Italy, Netherlands, Switzerland, United Kingdom (UK) and US. All centres manage calls from health care providers. Australia, Italy, Germany, Switzerland and US manage calls from the public as well. Methylphenidate: Five of 7 countries reported an increase during the study period (range 17–137%; Table 1).

**Table 1.** Prescription stimulant exposures reported to poison centres from 2007–2010.

Country in % Change Rank Order	Exposure rate per 100,000 population				Rate change (first rate reported to 2010)	% change (first rate reported to 2010)
	2007	2008	2009	2010		
<b>METHYLPHENIDATE</b>						
United States	1.043	2.406	2.381	2.468	+1.425	+137%
Netherlands	2.202	2.730	2.717	3.578	+1.376	+63%
Australia	1.643	1.561	2.140	2.328	+0.685	+42%
Switzerland	1.734	1.662	2.301	2.427	+0.693	+40%
Germany	0.742	0.826	0.833	0.871	+0.129	+17%
United Kingdom	NR	0.355	0.352	0.257	−0.099	−28%
Italy	0.000	0.000	0.007	0.003	+0.003	–
<b>AMFETAMINE</b>						
United States	1.171	2.885	3.181	3.756	+2.586	+221%
Netherlands	0.734	0.853	0.728	0.983	+0.250	+34%
Australia	0.776	0.895	0.875	0.916	+0.140	+18%
United Kingdom	NR	0.162	0.171	0.149	−0.013	−8%
Germany	0.030	0.030	0.045	0.023	−0.008	−25%
Italy	0.015	0.015	0.013	0.008	−0.007	−45%
Switzerland	NR	NR	NR	NR	–	–

NR = not reported.

The UK reported a decrease of 28%. Amphetamine: US reported the highest rate and surpassed second ranked Netherlands by almost 4-fold. While US, Netherlands and Australia reported increased amphetamine rates (range 18–221%), the remaining countries suggesting a downward trend from 8 to 45%. There are no prescription amphetamines available in Switzerland. **Conclusions:** Methylphenidate exposures per person increased in the majority of participating countries. Amphetamine exposures were less commonly reported to participating non-US centres, which indicated less than 50% change during the study period. While these data illustrate rates over time within each country, one cannot compare rates between countries due to variation of data collection methods (some centres accept calls from the public, some do not). Additional data is required on reporting bias, drug availability, drug supply source, and perhaps cultural differences that may contribute to these findings.

#### 75. Mushroom Poisoning in the UK: Review of Enquiries Received by the National Poisons Information Service

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**Objective:** To assess the epidemiology of mushroom poisoning in the United Kingdom between January 2008 and 14th November 2011. **Methods:** Enquiries to the National Poisons Information service were reviewed retrospectively and analysed to evaluate patterns of exposure. **Results:** A total of 946 enquiries were analysed; this accounted for 0.4%, 0.37%, 0.63% and 0.52% of all enquiries in 2008, 2009, 2010 and 2011 respectively. Fifty-four percent (n = 515) of the total involved children under 15 years and 45% (424) involved children < 5 years. In this group 81% were reported to have ingested an unidentified mushroom; 77% were asymptomatic, 12% reported gastrointestinal symptoms only and 4 cases developed moderate features. Eighty-four percent of all enquiries occurred between June and

November (peak in September) indicating a possible influence of climatic conditions on growth. Enquiries that reported symptoms either at time of enquiry or at follow-up were reviewed to determine the time of onset of symptoms. Of these (n = 332) 126 were excluded due to insufficient detail on the record or unconfirmed exposure. In the remaining 206 enquiries, 72% reported symptoms within the first 6 hours with 28% reporting later onset of symptoms. In the under 5 age group who reported symptoms only 34 enquiries contained sufficient data to determine time of onset and in that group only 2 developed features later than 6 hours post ingestion. None of those followed up developed severe features. Forty (5%) cases had a poisoning severity score of moderate or severe. In this group 21 were regarding an unknown species, 9 concerned psilocybin or magic mushrooms and the other 10 were regarding known species of mushroom including *Amanita* and *Cortinarius* species. **Conclusion:** Seasonal poisoning is not a new phenomenon; the suggestion that availability is a major determinant in the risk of poisoning particularly in children is supported by these data. Foragers and pickers who consume larger quantities of mushrooms tend to develop more severe symptoms. Education of the public concerning consumption of mushrooms and education of health personnel regarding early treatment and transfer to hospitals with appropriate facilities are important for improving outcome.

#### 76. Ocular Exposures: A Scottish View

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**Objective:** To review contacts to a poisons centre relating to eye contact. **Methods:** A retrospective review of poisons centre data, recording agents involved and comparing demographics, poisoning severity score (PSS) and predicted risk with general call load. **Results:** 443 contacts involving ocular exposure were identified between January 2004 and December 2010, representing 3.5% (443/12685) of our enquiries

over this period. Patient ages ranged from 11 days to 92 years. Two hundred and fifty-six patients were male, 177 female; in 3 cases the patient's gender was unknown and in 7 cases it was not recorded. A variety of products were involved in calls relating to eye contact, including concentrated laundry detergent pouches ('Liquitabs®'); bleaches and other cleaning products; an inhalant containing a mixture of essential oils (Oilbas Oil®); automotive products including petrol or diesel fuel and hydraulic oil. Many products appear only once in calls during this series. Common enquiries included calls related to agents known to be injurious to the eye (for example CS or pepper spray, chilli peppers). Another common theme in enquiries was calls involving products perhaps more likely to get into the eye (for example aerosol deodorant products, Liquitabs®). Comparison of PSS for eye contact enquiries with [all enquiries] is as follows: no symptoms (PSS0) 17.15% [52.06%], minor (PSS1) 62.07% [27.53%], moderate (PSS2) 11.74% [6.87%], severe (PSS3) 0.22% [1.89%]. Enquiries were also analysed regarding the predicted risk of the exposure: Non toxic 0.23% [6.53%], Probably non toxic 19.86% [44.35%], Poisoning not excluded 66.59% [39.04%], Predictable risk 0.23% [1.21%], Confirmed toxicity 12.19% [6.53%].  $\chi^2$  statistical analysis gives  $p < 0.001$  for both groups. **Discussion:** We found an apparent bias towards more symptomatic patients in this case series, as assessed by poisoning severity score; this may be because patients who have no initial symptoms 'self-select' and do not seek treatment. However comparison of perceived toxic risk of these exposures suggests that calls involving eye contact have a greater potential toxic risk than our background call load. **Conclusion:** Poisons centres continue to receive calls involving eye contact. Information on commonly-encountered product types can be targeted to address the potential toxic risks due to ocular exposure.

#### 77. Toward Harmonisation of National Poisons Information Service and National Poison Data System Reporting

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**Objective:** The National Poisons Information Service (NPIS) in the UK and the National Poison Data System (NPDS) in the US each publish an annual report. While the goals of these reports are similar, the analyses and displays are quite disparate. **Methods:** We chose 3 data analyses from the 2010/2011 NPIS report and developed corresponding analyses for NPDS data. Where available we examined NPIS data for telephone enquiries (UK-Phone) and sessions with the computer data system (UK-TOXBASE), and the sum (UK-Both). Since NPIS receives queries only from health care professionals, we divided NPDS data (US-Total) into calls from health care facilities (US-HCF) and (US-nonHCF). We compared these UK and US measures graphically and statistically (scatter plots and correlation coefficients). **Results:** Table 1 lists the figures analyzed and results. **Conclusion:** Direct comparisons of NPIS and NPDS data were accomplished with some modest adjustments to time intervals and sub-setting of NPDS enquiries. Both the temporal

**Table 1.** Comparison of NPIS and NPDS enquiries.

NPIS Figure	Type of Display	UK Encounters	US Encounters	Best correlation
3.1 Telephone enquiries and TOXBASE sessions from 2000 to 2010/11	Change over time	UK-Phone = 1.19m UK-TOXBASE = 3.96m UK-Both = 5.15m	US-HCF = 3.98m US-non HCF = 22.2m US-Total = 26.2m	UK-TOXBASE v US-HCF r = 0.973 (N = 11)
3.3 Age of poisoned patients reported in telephone enquiries	Patient demographic	UK-Phone = 50,767	US-HCF = 2.38m US-non HCF = 1.95m US-Total = 0.424m	UK-Phone v US-Total r = 0.937 (N = 10)
5.6 Number of CO enquiries by month 2009/10 and 2010/11	Specific exposure by month	UK-Phone = 576	US-HCF = 7,953 US-non HCF = 19,425 US-Total = 27,378	UK-Phone v US-HCF r = 0.652 (N = 24)

N.B: Where necessary, we used the UK financial year for NPDS intervals created, compared the total numbers of encounters, and reported the most highly correlated measures (m=millions of Encounters).

patterns and the demography of patients were similar (i.e. age and gender). NPIS data provides a comparison between access to toxicological information and advice according to computer access (TOXBASE) and phone access. NPDS encounter data is from both health care professional and consumer calls. There are many potential benefits for the international standardization and harmonization of reporting poison enquiries.

#### 78. Poisonings in the Nordic Countries in 2007: A 5-Year Epidemiological Follow-Up

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**Objective:** To map mortality and morbidity of poisonings in Denmark, Finland, Iceland, Norway and Sweden in 2007 and undertake a comparison with a corresponding study in 2002.<sup>1</sup> **Methods:** Morbidity was, as for 2002, defined as acute poisoning (ICD-10 codes, main and side diagnoses) treated in hospitals. The figures were extracted from the National Patient/Hospital Registers. Deaths recorded as acute poisoning (using the same ICD-10 codes) were collected from the National Cause of Death Registers. **Results:** Annual mortality of acute poisonings per 100,000 inhabitants (rate) for 2007 was 22.4 in Finland representing a significant increase from 2002. The increase was chiefly due to a change in coding of alcohol, but also represented a real increase in fatal alcohol intoxications. The poisoning death rate in the other Nordic countries varied between 8–13 and was at the same level as for 2002. The morbidity rates for 2007, between 158–285 per 100,000 inhabitants, represented a slight increase compared to 2002 figures. **Conclusion:** The increase in poisoning death rate for alcohol and thus total rate in Finland in 2007, compared to 2002, has further increased the gap to the other Nordic countries. Poisoning morbidity rates in the Nordic countries are at the same level, but the variability shown indicates that more harmonization and collaboration is needed to increase the data quality. **Reference:** 1. Andrew E, Irestedt B, Hurri T, et al. Mortality and morbidity of poisonings in the Nordic countries in 2002. *Clin Toxicol (Phila)* 2008; 46:310–3.

#### 79. Incidence of Poisoning in Rafsanjan, Iran

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**Objective:** The purpose of this study was to characterize the poisoning cases admitted to the emergency department of Ali-Ebne Abitaleb hospital from April 2009 to June 2009, Rafsanjan, Iran. **Methods:** The above mentioned patients were examined upon their arrival to the emergency department and hospitalized for further treatment. Data concerning these patients was collected from the emergency department as well as other units and analysed. **Results:** 125 patients with poisoning were referred to the emergency department. 42.4% of the patients admitted to the emergency department were male and 57.6% were female. The age of the male patients was in the range of 18–53 and the age of female patients was in the range of 16–50 years; 55.2% of the cases were from the age group 20–29 years. Most poisonings were intentional. The most important agents of poisoning were drugs (55%), especially sedative-hypnotic drugs, followed by opioids (15%) and pesticides, especially organophosphates, endosulfan and amitraz (28%). 97.6% of the hospitalized patients could be discharged after 2–5 days, but 2.4% of patients died. Two of the patients died after endosulfan poisoning and one after organophosphate poisoning. Naloxone for opium, atropine, pralidoxime for organophosphate and thiopental for endosulfan were prescribed for the patients. Respiratory depression, apnea, loss of consciousness and status epilepticus were important and severe signs of these poisonings. **Conclusion:** The majority of poisoning cases in Rafsanjan area involves drug poisoning especially sedative-hypnotic drugs, and pesticides. Good treatment and management of patients in the emergency department increase survival rate, and therefore poisoning units and expert physicians should be available to the emergency department.

#### 80. Occurrence of Poisoning over 50 Years Treated in the Munich Center

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**Objective:** How did the pattern of poisonings develop over the last 50 years in Munich? **Methods:** All cases treated in the years 1964, 1974, 1984, 1995, 2010 were exploited. **Results:** Cases are given by the year. Sedatives-hypnotics: In 1964 methylprylon came first with 116 cases, as did carbromal in 1974 (109). 1964–1995:

barbiturates decreasing from 92 to 20, all 3 have now disappeared. In 1974–2010 diphenhydramine poisonings occurred 26 times to 42. Benzodiazepines started in 1964 (17) and peaked in 1995 (285), still high in 2010 (216). Zopiclone/zolpidem began in 1995 (6) and went up to 49 in 2010. Analgesics: stayed at the same level but changed from pyrazalons to paracetamol and NSAIDs (44–60). Neuroleptics: few cases occurred between 1964 and 1995 (12–24) but went up to 65 in 2010 due to quetiapine. Tricyclic antidepressants (TCA): start in 1964 (4) increased to 59 in 2010. Heroin commenced in 1964 (1), peaked in 1995 (195), still high in 2010 (119). Cocaine started in 1974 (1), went up to 34 in 2010. Methadone went up from zero in 1985 to 64 in 2010. Environmental patients were first seen in 1995 (156), coming down to 5 in 2010. Chemicals: carbon monoxide: 24 in 1964, still 19 in 2010. Lead (20) and paraquat (7) had a peak in 1974, organophosphates in 1984 (9). Cause of death: paraquat 9/10 (90%), parathion 5/15 (33.3%), arsenic 2/18 (18.1%), barbiturates 10/238 (4.2%), carbromal 5/133 (3.8%), TCA 4/154 (2.5%), cocaine 2/115 (1.7%), benzodiazepines 5/908 (0.55%). **Conclusion:** Sedative-hypnotics have become safer. Poisonings by analgesics had no fatalities. Intoxications with neuroleptics increased due to quetiapine. TCA intoxications are still high and dangerous. Heroin intoxications are decreasing as methadone-intoxications are increasing. We had no in-hospital deaths from heroin or methadone but two from cocaine. Environmental problems had hype in the 90s. Chemicals were always the number one killer.

#### 81. Drug Abuse in Pediatrics: Increasing Trend in 15 Years Experience of Pavia Poison Centre

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**Objective:** To evaluate the abused substances in different age-groups during a 15 year period in selected pediatric cases. **Methods:** A retrospective analysis of selected pediatric patients (age 10–17) referred to Pavia Poison Centre (PPC) from 1996–2010 was performed: patients with a positive history of substance abuse were included. The substances involved have been correlated with two age groups (10–13 and 14–17 years old) during three time periods (period 1: 1996–2000; period 2: 2001–2005; period 3: 2006–2010). **Case series:** From 1996–2010, among 5,322 patients aged 10–17, 349 (6.5%) presented with a positive history of abuse (31 in period 1, 116 in period 2, 202 in

period 3). The substances of abuse involved were ethanol (143; 41%), tetrahydrocannabinol (THC) (70; 20%), hallucinogens/LSD/ketamine (27; 7.7%), amphetamines (21; 6%), cocaine (12; 3.4%), opiates (9; 2.6%), other substances (8; 2.3%), unknown substances (59; 17%). A progressive increase in THC consumption (3.2%, 16.4% and 24.8%), hallucinogens (3.2%, 5.2% and 10%) and cocaine (0%, 3.4% and 4%) was observed through periods 1, 2 and 3 respectively. A decrease in ethanol (56% versus 33%) and opiates abuse (3.4% versus 2.5%) was registered through period 2 and 3 respectively. A decrease in PPC admission for unknown substances was shown from period 1 to 2 (55% versus 8.6%), followed by an increase in period 3 (15.8%). Among 349 consumers, those aged 10–13 and 14–17 represented 13% (45/349) and 87% (304/349) respectively. Patients aged 10–13 years increased from 6.4% to 15.3% from 1996 to 2010; among these a particular rise in THC consumption during the last 5 years was observed. **Conclusion:** In our experience consumption of drugs of abuse has been increasing during the last 15 years in patients aged 10 to 17. Patients aged 14–17 represent the major part of consumers for all the evaluated substances; however an increase in THC abuse was observed in 10–13 year-old consumers during the last five years. The increase of unknown substances at PPC admission in the last five years may be related to the availability of the new drugs of abuse.

### 82. The Epidemiological Profile of Methotrexate Enquiries to the National Poisons Information Centre of Ireland

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**Objective:** To characterise the epidemiological profile of methotrexate enquiries to the National Poisons Information Centre (NPIC). **Methods:** A retrospective observational review of telephone enquiries to the NPIC from 1st January 2004 to 31st December 2010 was conducted. Enquiries relating to methotrexate were extracted from the NPIC database. Data on patient demographics, enquiry source, circumstances, and treatment recommended were collated. National guidelines for pharmacists recommending dispensing of only 2.5 mg tablets were introduced in 2008. The number of cases where 10 mg strength tablets were reported was determined before and after 2008. **Results:** During the study period, the NPIC received 131 telephone enquiries relating to methotrexate exposure in 88 patients (31 males, 53 females, 4 patients of unspecified gender) and 1 veterinary enquiry. There were 13 paediatric cases (mean age 3.69 years, range 1–12 years) and 75 patients aged  $\geq 14$  years (mean age 54.7 years, range 14–93 years). Exposure data were available for 87 patients and there was one request for information on folic acid administration. Review of 87 cases revealed that oral exposures predominated (tablets  $n = 85$ , oral solution  $n = 1$ ) and there was one case of methotrexate injection. The circumstances of the exposures were (i) therapeutic error ( $n = 58$ , 66.7%), (ii) deliberate overdose ( $n = 17$ , 19.5%), (iii) accidental ingestion ( $n = 11$ , 12.6%), (IV) adverse drug reaction ( $n = 1$ ). Enquiries originated from hospitals ( $n = 31$ , 35.63%), general practitioners (GP) ( $n = 26$ , 29.89%), community pharmacists ( $n = 23$ , 26.44%), and members of the public ( $n = 7$ , 8.04%). Twenty-eight (32.18%) patients were referred to an emergency department, 16 (18.39%) were referred to a GP, 4 patients did not require medical assessment. Supportive care was recommended for 39 (44.83%) patients already undergoing assessment in a healthcare facility. Overall, 10 mg and 2.5 mg strength tablets were implicated in 21 (24.7%) and 18 (21.2%)

cases respectively. Tablet strength was not specified for 46 cases. Prior to 2008, 10 mg tablets were reported for 9/42 (21.4%) cases and following 2008, 10 mg tablets were reported for 12/43 (27.9%) cases. **Conclusion:** Methotrexate enquiries fell into 3 main categories; therapeutic error, deliberate overdose, and accidental paediatric exposures. 10 mg tablets were involved in  $> 25\%$  of cases reported to the NPIC since national guidelines were introduced in 2008.

### 83. Surveillance of Paraquat Cases Reported to the National Poisons Information Centre of Ireland: 1999–2011

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**Objective:** In July 2007, the Court of First Instance of the European Communities annulled the directive authorizing paraquat as an active plant protection substance. The aim of this study was to profile the epidemiology of paraquat poisoning by ingestion over a 13-year period and examine if the court ruling had an observable effect. **Methods:** A prospective observational study on cases reported to the National Poisons Information Centre (NPIC), involving the ingestion of paraquat-containing products was conducted from 1999–2011. Data on patient demographics, the circumstances of the exposure, product formulation (professional versus non-professional), clinical features, and mortality rate were collated. The number of cases of paraquat ingestion was determined for the period before and after the European ban was introduced. **Results:** The NPIC was consulted on the management of 105 patients who ingested paraquat-containing products during the study period. Overall, there were 25 cases of accidental poisoning (11 adults, 14 children  $< 14$  years). Fourteen (56%) of these patients accidentally ingested a professional/concentrated product, 8 ingested a non-professional product, and the product formulation was unknown in 3 cases. 12/25 (48%) patients were symptomatic, 12 were asymptomatic, and clinical features were unknown for one patient. There were 3 fatalities following accidental ingestion and all involved a professional product. Deliberate poisoning was reported for 80 cases (79 adults, 1 teenager aged 14 years). 37/80 (46.3%) patients ingested a professional/concentrated product, 22 ingested a non-professional product and the product formulation was unknown in 21 cases. 68/80 (85%) patients were symptomatic, 10 patients were asymptomatic, and clinical features were unknown for 2 patients. There were 34 fatalities (42.5% mortality) following deliberate poisoning and a professional product was implicated in at least 24 of these fatal cases. Between 1999 and 2007, there were 96 poisoning cases reported to the NPIC. Following the European ban, 9 poisoning cases were reported between 2008 and 2011. **Conclusion:** Deliberate ingestion of paraquat-containing products was associated with a 42.5% mortality rate. A professional formulation product was known to have been ingested in 27/37 fatal cases. The number of cases of paraquat poisoning decreased dramatically after European ban was introduced in 2007.

### 84. Analysis of Poisoning in Children less than 6 Years old Reported to the Poison Control Center in Palestine

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**Objective:** To analyze and shed light on phone calls received by the Palestinian Poison and Drug Information Center (PCDIC) regarding poisoning in children less than 6 years of age. **Methods:** All data regarding children less than 6 years old, received by the PCDIC since its establishment in 2006 till now were analyzed. Analysis was performed using SPSS 16. **Results:** A total of 628 inquiries were received with an average age of  $2.7 \pm 1.3$  years. More than half of the calls (63.2%) were received from health care providers. More than two thirds (77.2%) of the inquiries were regarding males, and the majority (89.4%) of the inquiries were regarding poisoning, the rest were about drug information. Medications were encountered in the majority (52.0%) of cases, followed by cleaning products (17%). The rest were pesticides, plants and others. Most (98.9%) of the cases were due to a single agent. Calls were received all day long, but mostly from 12:00–18:00 hrs (45%), followed by 18:00–24:00 hrs (37.3%). Most families brought their children within a few hours of poisoning, and the route of poison entry was oral in 93.3%. In most cases, the poison center was contacted before any symptoms developed (63.4%). In the rest of the cases varied symptoms had developed from vomiting, abdominal pain, to tachycardia, bronch-orrhea, to CNS depression; one child developed coma. At the hospital, and before calling the poison center, 87 children (13.8%) received gastric lavage, and only one child received activated charcoal. After the poison center was contacted, charcoal was advised in 22 cases, lavage in only 4 cases. The rest received no treatment, were given antidotes or were kept under observation. **Conclusion:** Poisoning of children in Palestine is common, and more attention should be given to parent and child education to avoid poisoning. Chemicals should be safely stored at home, and away from reach and sight of children. Continuous medical education is needed for health care providers regarding the management of acute poisoning cases. The use of gastric lavage should be decreased and limited to life-saving cases, while the utilization of activated charcoal should be encouraged.

### 85. Prevalence of Caving Accidents Due to “Bad Air”

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**Objective:** Caving is a demanding sport widely practiced throughout the world. While data is collected on yearly caving accidents in various countries, no study has analyzed injury type to help establish appropriate medical rescue protocols in these austere environments. This study was performed to examine the number of reported incidents of caver exposure to “bad air” (defined as poor quality air due to such toxins as carbon dioxide, methane, hydrogen sulfide) in the U.S. over the past 3 decades. **Methods:** A retrospective analysis of caving incidents in the U.S. from 1980 to 2008 was performed using data collected and documented by the National Speleological Society – American Caving Accidents annual publication. This publication includes case reports voluntarily provided to the National Speleological Society by groups such as local caving grottos and emergency medical service providers. Data were extracted and recorded by individually reviewing each yearly publication. Each victim and the associated circumstances were examined. Victims of all ages who required rescue while caving and for which a report was generated within the U.S. were included. For each incident, the victim gender, year, location, incident type, rescue type, and the final outcome were recorded. **Results:** There were a total of 1,356 cavers

requiring assistance from a total of 877 reports identified from 1980 to 2008. Of these, 23 cases (1.6%) were due to "bad air". The majority involved males (87%). There were 2 deaths (8.6%) reported, with the remainder reporting no permanent consequences. Self extrication from the cave occurred with 19 (82%) of the cases, with the remainder requiring emergency medical services. *Conclusion:* Prior to this study, there has been no extensive analysis of injuries involved with caving. Cave rescue is often a complex and time consuming endeavor. Though rare, both cavers and rescuers need to be aware of the potential dangers associated with poor quality cave air. Considerations should be made to appropriate detection and proper use of personnel protective equipment during cave rescue incidents.

#### 86. Do Referral Hospitals Provide Valid Toxicovigilance Signals for Acute Poisoning in Rural Sri Lanka?

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*Objective:* Acute poisoning is a major public health issue in the developing world. Most poisoning occurs in rural areas where patients receive their initial treatment in small peripheral hospitals before being transferred to secondary care hospitals. The aim of this study was to determine what data on acute poisoning admissions would be most representative of the true acute poisoning epidemiology in the district. *Methods:* A prospective study of all patients above the age of 12 admitted following poison ingestion was conducted from September 2008 to January 2010 in all hospitals with inpatient facilities in the Anuradhapura district of North Central Province of Sri Lanka. In the primary rural hospitals, data was extracted using structured queries from patient charts. In the referral hospital, data was collected prospectively by research assistants. Referred patients were identified using a simple algorithm based on date, name and age. The 'observed' estimates of the incidence, demographics, type and case-fatality of poisoning that would be found by studies using primary hospitals, referral hospitals, and 'all admissions' (i.e. double counting transfers), were compared with the 'expected' or most accurate method to measure the epidemiology of poisoning. *Results:* There were 3813 poisoned patients admitted to all the hospitals in Anuradhapura district in Sri Lanka during 17 months study period. Of these 3111 first presented to a rural hospital; 2272 were transferred to referral hospital. Seven hundred and two patients presented directly to the referral hospital. There was no substantial difference in the age/gender profile in any data set. The secondary referral hospital data provided the closest estimate to the true epidemiology for the pattern of poisoning, total fatalities and case-fatality (when compared to a primary hospital data set and an "all admissions" data set that duplicated data on transfers). *Conclusion:* The age and gender distribution, epidemiology and pattern of poisoning and case fatality data from secondary referral hospitals are very close to those found with far more labour-intensive methods for studying epidemiology of poisoning using data linkage to track transferred patients. Such data provide

an economical way to accurately estimate changes over time in the pattern and severity of poisoning.

#### 87. Recent Rise in Finland of Accidental Poisonings from Medications

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*Objective:* To study and compare fatal, alcohol and drug intoxications in Finland during the years 2004–2009. Subgroups of cases, which occurred outside hospitals and those which occurred in hospitals were compared. *Methods:* All post-mortem toxicological investigation in Finland is centralised at the Department of Forensic Medicine, University of Helsinki. From that database the cause and place of death as well as the age and sex of the deceased for each fatal poisoning were examined separately. The fatal cases were classified as suicides if there was a farewell note or some other clear message from the patient. The rest of the cases were classified as accidents. *Results:* The number of fatal poisonings, including suicides, remained unchanged: 1200 cases annually (22/100,000 inhabitants). The number of patients dying in hospitals due to poisoning varied between 50–70/year. The number of fatal accidental drug poisonings has risen from 191 in 2004 to 341 in 2009 whereas alcohol poisonings have diminished from 542 in 2004 to 432 in 2009; the changes were significant  $p < 0.001$ . Suicides due to poisoning were almost always committed by taking an overdose of drugs and the total number varied between 276 (in 2008) and 341 (in 2006). Also, agents causing the poisonings changed. In accidental poisonings medicines are more common year after year. In particular, the number of deaths due to opioids rose from 135 (in 2004) to 189 (in 2009), whereas paracetamol still plays a minimal role in Finland. Furthermore, alcohol has either remained at the same level (cases with death outside hospitals) or even decreased (death in hospitals). *Conclusion:* The total number of fatal poisonings divided into accidental cases and suicides was stable during the study years. There were, however, significant changes in causative agents concerning accidental poisonings. The number of fatal accidental alcohol poisonings peaked in 2004. That year several political decisions, like the free import of alcohol, increased the consumption of alcohol. Since then, alcohol poisonings have happily diminished. On the other hand, fatal accidental drug poisonings have shown a significant rise without any single cause which could be removed and this should evoke concern.

#### 88. Eye Exposure Inquiries to the New Zealand Centre: A 5 Year Survey

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*Objective:* To describe the epidemiology of human eye exposure inquiries to the New Zealand Centre over a 5 year period. *Methods:* A retrospective survey (July 2006 to June 2011) of telephone inquiries involving eye exposures was undertaken. Patient demographics; product names, categories and corrosive potency; exposure characteristics and initial treatment advice were collated. *Results:* 173,236 inquiries were received with 6,780 (yearly average 3.9%, range 3.7 to 4.5%) related to eye exposures (53% males, 45% females).

The main chemical groups involved were household cleaners (22.0%), industrial products (13.7%), cosmetics (10.5%), and with lower frequency topical therapeutics (4.8%), miscellaneous household products (4.6%), paints (4.4%), insecticides (3.9%), plants and laundry products (both 3.7%), fuels (3.1%) and herbicides (2.7%). Fifty-nine per cent of plant exposures (33% euphorbia) were classified as severely irritant or corrosive. Liquids, mists and sprays accounted for 84% of exposures, the majority in the home (79%), 62% in adults and 38% in children. Most inquiries occurred between 0800 and 2300 hours with peaks at 1100 to 1200 hours and 1700 to 1800 hours for home exposures, and at 1000 to 1100 hours and 1500 to 1600 hours for workplace exposures. Sixty-one per cent of calls came from homes, 28% from medical facilities, and 12% from workplaces. Corrosive or potentially corrosive substances (mainly alkaline household and industrial detergents and cleaners) accounted for 24.7% of inquiries. Inquiries related to corrosives (765) were more predominant in the home (446) than the workplace (242). For the period 2008 to 2011, medical referral was recommended in 57% of chemical exposures, involving mainly severely irritant or corrosive substances (41%) as well as a significant proportion (34%) of mild to moderate irritant substances for which medical referral would not be automatically recommended. *Conclusion:* Human eye exposure inquiries to the New Zealand Centre are a significant proportion of total calls. Most inquiries relate to adult exposures in the home, occupational exposure inquiries being much less common. Modification of product ingredients to non-corrosive or less irritant formulations may reduce the severity of eye exposure outcomes but may not necessarily result in fewer referrals to medical facilities.

#### 89. Ingestions and Poisoning in Children Presenting to a UK Emergency Department: Changes over 30 Years

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*Objective:* To determine the incidence of ingestions and poisoning in children presenting to a UK Emergency Department (ED) and to identify the commonly occurring substances, and compare these to similar data collected in the same hospital in 1979<sup>1</sup>. *Methods:* Children presenting with an actual or suspected ingestion, poisoning or overdose to the ED of the Royal Victoria Infirmary, Newcastle upon Tyne in 2010 were identified retrospectively from the ED information system. Medical notes were examined and demographic details, substance responsible, symptoms and management were extracted and analysed. *Results:* A total of 252 events with potential toxicological diagnoses were identified in 248 children (aged  $\leq 15$  years) accounting for 1.75% of all ED attendances in 2010. Ninety-eight attendances were for children aged  $\leq 4$  years; 43 due to medicinal substances, most commonly accidental ingestion of paracetamol. Twenty-two (22%) of these children were admitted, usually for 4–6 hours observation or to await blood test results only. One hundred and thirty-six children aged 12–15 years attended with ingestions or overdoses, accounting for over 1 in 20 of the ED attendances in this age group. Eighty-three of these older children attended having drunk excess alcohol; 36 had taken a medication as part of an attempt at deliberate self harm, most commonly paracetamol; and 12 had taken illicit drugs. Forty-eight (35%) were admitted, mostly due to

deliberate self harm. Only 2 children suffered symptoms graded as severe; the remainder had only mild to moderate problems. **Conclusion:** Ingestions and poisonings in children remain a significant part of the workload of emergency departments. Fewer young children need admission compared to similar data collected in the same hospital in 1979, with a virtual disappearance of problems due to salicylate, tricyclic antidepressant, benzodiazepine and iron ingestions. Excess alcohol and ingestions related to deliberate self harm in young people (aged 12–15 years) remain a significant problem. **Reference:** 1. Lawson GR, Craft AW, Jackson RH. Changing pattern of poisoning in children in Newcastle, 1974–1981. *Br Med J (Clin Res Ed)* 1983; 287:15–7.

#### 90. Carbon Monoxide Enquiries Reported to the UK National Poisons Information Service Units between April 2009–March 2011

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**Objective:** To ascertain the number and type of enquiries regarding carbon monoxide exposure reported to the UK National Poisons Information Service (NPIS). **Methods:** The study involved the retrospective analysis of data collected between 1 April 2009 and 31 March 2011. **Results:** The NPIS received 566 telephone enquiries regarding confirmed or suspected carbon monoxide exposures over this period. Most enquiries (478 of 566) involved carbon monoxide exposure at home; 39 occurred in the workplace, 24 in a public area, one was at a hospital and the exposure location was unknown in 24. The suspected source of carbon monoxide in the domestic setting is known in 339 of 478 cases; central heating boilers were implicated most often (accounting for 159 of 339 enquiries). In 121 of the 566 enquiries multiple individuals were involved, so that the total number of patients was at least 828 (52.8% were female and there was a preponderance of children < 10 years). The maximum number of individuals exposed in a single incident was 17 and involved residents in rented accommodation that had a faulty central heating boiler. The poisoning severity score (PSS) was known in 689 patients; 644 patients had a PSS of 0 or 1 (minor toxicity); 27 had features of moderate toxicity (PSS 2), 18 were graded PSS 3 (severe toxicity); no PSS was available in the remaining 139 patients. Carboxyhaemoglobin concentrations were known in 241 of 828 patients (mean ( $\pm$  SD) 11.7  $\pm$  11.4%). The mean ( $\pm$  SD) carboxyhaemoglobin concentration in 17 of the 18 severe cases (PSS 3) was 29.7  $\pm$  14.8% and three patients died. Exposure was accidental in 769 cases, 25 were deemed intentional and the intent was uncertain in 34. Eighteen of the 25 intentional exposures involved vehicle exhaust fumes, three involved the lighting of a barbecue in a confined space, one involved a house fire, one involved the inhalation of carbon monoxide from a cylinder and the sources in the two remaining exposures were unknown. The mean ( $\pm$  SD) carboxyhaemoglobin concentration in 20 of these 25 intentional exposures was 20.4  $\pm$  13.7%. **Conclusion:** Carbon monoxide poisoning remains an important preventable cause of morbidity and mortality in the UK.

#### 91. School – A Safe Place to Learn and Play?

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**Objective:** The foundation stage/phase was introduced into the primary schools of England and Wales in September 2008. Government guidelines recommend a whole school approach (ages 3–11) to an ethos of learning which includes using the outdoors as a learning environment alongside traditional classroom-based education. Students are encouraged to learn by direct, hands-on experience through play and pupil-led investigations and consequently they have access to a much larger variety of potentially toxic agents and plants. **Methods:** Enquiries to NPIS between 1st September 2009 and 31st August 2011 relating to exposures of children (ages 3–11) to potentially toxic materials in schools were analysed with regard to type of material involved and severity of symptoms. **Results:** A total of 574 enquiries were received during the study period, 37.5% involving girls and 61.5% involving boys. Children aged five were the subject of the highest number (17.6%) of enquiries. The most common agents involved in exposures to pupils were plants (leaves, flowers, seeds and nuts), low toxicity miscellaneous products, chemicals, ice packs (food), cleaning products and pharmaceuticals. Although the majority of exposures resulted in minimal symptoms only, 12.7% of enquiries from schools required referral to hospital for treatment and a further 24% of enquiries were from hospital where the child had already been admitted. Some of the more serious cases involved exposure to agents such as isopropyl methyl sodium hydroxide, unused EpiPens (epinephrine auto-injector) and rat bait. **Conclusion:** Schools are encouraged to provide a new learning experience for pupils but should ensure that a comprehensive risk assessment is carried out on all materials, including plants, to which children might become exposed. Do NPIS centre staff have a role to play in providing expert poisoning-prevention education to schools?

#### 92. Ranitidine Overdose in Paediatric Patients

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**Objective:** To investigate the circumstances and etiology of ranitidine overdose in patients aged under 3 years old reported to the UK National Poisons Information Service (NPIS) between November 2008 and October 2011. Disproportionately high levels of therapeutic error have been noted during calls to NPIS centres. The causes of this are investigated. **Methods:** Using data extracted from UKPID, a centralised NPIS telephone enquiry database, we reviewed the number and nature of incidents involving ranitidine from November 2008 to October 2011. **Results:** 244 calls were made to the NPIS between 01/11/2008 and 31/10/2011 regarding poisoning with ranitidine alone. One hundred and ninety-six incidents (80.3%) involved children aged under 3 and 205 (84.0%) involved children aged under 5; by contrast, in the financial year 2010–2011, only 28.8% of all calls made to the NPIS involved children aged under 5 ( $p < 0.0001$ ). In those patients aged under 3, 86.7% (170/196) of ranitidine overdoses were due to therapeutic error, compared to 7.0% of all calls for the same age group taken in the same time period ( $p < 0.0001$ ). Of those patients who overdosed as a result of therapeutic error, 146 (85.9%) ingested ranitidine syrup, and 43 of these patients (29.5%) were given a 10 times overdose of 75 mg/5 mL syrup. Medical intervention was required in 19.4% (38/196) of all patients under 3, most commonly investigations (16/38 or 42.1% of

patients). 11/196 patients (5.6%) were referred to A&E and 12/196 patients (6.1%) were referred to their GP. 85.2% (167/196) patients were asymptomatic; 10.2% (20/196) patients had minor features, and 1 patient (0.5%) had moderate features (multiple episodes of vomiting and diarrhoea). **Conclusion:** Ranitidine overdose is a common enquiry to the NPIS. Although usually asymptomatic these cases often required some sort of medical intervention. Cases frequently involved paediatric patients. Overdose commonly occurred due to administration of 10x the prescribed dose of ranitidine syrup, suggesting a preventable dosing error by carers. Although the consequences of ranitidine overdose are usually benign, these results suggest that formulation changes could reduce risk and prevent unnecessary presentations to health professionals.

#### 93. Changing Epidemiology Patterns of Deliberate Self Poisoning in Rural Sri Lanka

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**Objective:** Acute poisoning is a major public health issue in many parts of the world. The epidemiology and the mortality rate are higher in low and middle income countries, including Sri Lanka. The aim of this study was to provide details about the epidemiology of acute poisoning in a rural Sri Lankan district and to identify the changing patterns and epidemiology of poisoning. **Methods:** A prospective study was conducted from September 2008 to January 2010 in all hospitals with inpatient facilities in Anuradhapura district of North Central Province of Sri Lanka. Acute poisoning data was extracted from patient charts. Selected data were compared to the data collected from a 2005 study in 28 hospitals. **Results:** There were 3813 poisoned patients admitted to the hospitals in the Anuradhapura district over 17 months. The annual population incidence was 404 poisoning cases per 100,000 population. The total number of male and female patients was approximately similar, but the age distribution differed by gender. There was a very high incidence of poisoning in females aged 15–19, with an estimated cumulative incidence of 6% over these five years. Although, pesticides are still the most common type of poison, pharmaceutical poisonings are now 21% of the total and have increased 1.6 fold since 2005. The increase in pharmaceutical poisoning has been associated with a decrease in oleander poisoning. **Conclusion:** Acute poisoning remains a major public health problem in rural Sri Lanka and pesticide poisoning remains the most important poison. However, cases of medicinal drug poisoning have recently dramatically increased. Youth in these rural communities remain very vulnerable to acute poisoning and the problem is so common that school-based primary prevention programs may be worthwhile.

#### 94. Intentional Poisonings in Elderly Patients

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**Objective:** Bulgaria is among the countries with the most rapidly aging population and among those with a high incidence of suicidal attempts by acute poisoning. The combination of physiological changes, occurring with age, and the high incidence of various chronic diseases with specific age-related behaviour changes, make these patients vulnerable and susceptible to attempting suicide. **Methods:** We present characteristics of intentional poisonings in the geriatric population, using 1) data from the clinico-epidemiological study of acute poisonings in patients over 60 from 1992 to 2003 in comparison with 2) data from the last two years 2009–2010. Methods of contemporary epidemiology for non-infectious diseases were used. Thorough examination of psychiatric and psychological state was performed and motives for committing suicide were analysed. **Results:** A total of 1551 patients over 60 years with acute poisonings were treated in the Toxicology Clinic during 10 years; representing 7.7% of all treated patients. Three hundred and fifty-one geriatric patients were hospitalized between 2009–2010; thus accounting for 8.2% of all hospitalized patients. Intentional poisonings were seen in 54% of these patients. Females (62%) prevailed over males (38%) and this trend was constant throughout the years. Moderate poisonings were most common among the intentional self poisonings (48%). Suicide attempts with medicines were most frequent (53%), with benzodiazepines being the most common products used for attempting suicide by self poisoning (33.8%). Among household products the most popular toxic substances were sodium hydroxide and cleansing products. The main reasons for attempting suicide in this age group were: 1) depression as a separate disease (31%); 2) various social and economic reasons (28%); 3) solitude and isolation from social/family life (21%); 4) chronic concomitant diseases, causing decreased vitality with impossibility of performing everyday activities without help (18.3%); 5) severe untreatable diseases (2.7%). **Conclusion:** We observed a rising trend in suicidal attempts in patients over 60 years. Suicidal poisonings prevailed in the acute intoxications in the elderly. Distinct differences in motivation of suicidal attempts among the young and elderly individuals were observed. Efforts must be made to reduce acute suicidal poisonings among the population aged over 60 years.

#### 95. Admissions to Intensive Care Unit Following Poisoning: A Ten-Year Study

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**Objective:** The correct management of some poisoned patients may require admission to the Intensive Care Unit (ICU). We studied the ICU use in poisoned patients and the related features. **Methods:** Ten year (July 1 2001– June 30 2011) prospective study including all patients admitted to our adult ICU with a main diagnosis of acute poisoning. We defined three criteria for ICU admission: the presence of vital function impairment (group 1); the perception that significant organ dysfunction could appear in asymptomatic patients on the basis of toxicokinetics or toxicodynamics (group 2); a clinical judgment for intensive observation in mildly symptomatic patients (group 3). **Results:** There were 107 poisoned patients (2.91% of admitted patients) and 60.7% were caused by miscellaneous agents. All toxic

agents were confirmed by toxicological laboratory analysis. The number of patients was 84 for group 1, 10 for group 2 and 13 for the third group. The average length of ICU stay (in days) was 3.9, 1.32 ( $P < 0.01$  compared to group 1 with Wilcoxon test) and 1.22 ( $P < 0.01$  compared to group 1), respectively. Eight patients died: three after paraquat ingestion, four due to a delay between poisoning and resuscitation (two 85-year-old patients for neurodepressant brain injury, one patient for heroin overdose and one for ethylene glycol), and one for aspiration pneumonia as a consequence of an organophosphate ingestion. For group 1 the poisons were mainly benzodiazepines, which were found at toxic levels in 45 patients. The main cause of vital function impairment was: respiratory failure requiring ventilatory support (82.1%), severe cardiovascular toxicity (6%), neurological dysfunction with a Glasgow Coma Score  $< 11$  (11.9%). Group 2 toxins were: paracetamol (3), acetonitrile (2), digoxin (2), paraquat (2) and ethylene glycol; only paraquat caused death. Patients in group 3 did not require ventilatory support and had a good recovery. **Conclusion:** A rational approach to ICU use is described: many poisonings (78.5%) presented an immediate life-threatening nature, while for patients who were asymptomatic or minimally symptomatic at admission, a short ICU stay was chosen for observation and treatment due the unpredictable clinical course.

#### 96. The TOXBASE® New Product and Unusual Cases Reporting Scheme – Naphyrone

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**Objective:** To describe alleged naphyrone exposures reported to The National Poisons Information Service Edinburgh Unit (NPIS) through the TOXBASE® new product and unusual cases reporting scheme. Naphyrone (naphthylpyrovalerone, O-2482, 1-(2-naphthyl)-2-(1-pyrrolidinyl)-1-pentanone) is one of a range of agents that have come to prominence in recent years, referred to in the UK as “legal highs”. However since 23 July 2010 naphyrone has been a controlled substance under the Misuse of Drugs Act 1971. Naphyrone is a naphthyl analogue of pyrovalerone that acts as a triple monoamine reuptake inhibitor, producing psychostimulant effects.<sup>1</sup> Naphyrone has close structural resemblance to the cathinones such as mephedrone. **Methods:** NPIS collects reports of exposure to new products and unusual cases through the UK national toxicology database TOXBASE®. These reports are submitted electronically by users via an on-line form. Reported cases were collated and analysed by NPIS. Confirmation of the agent involved by laboratory analysis was generally not available. It is possible that branded products may contain other ingredients. **Results:** 14 cases of alleged naphyrone exposure were reported between 19/4/2010 and 23/2/2011. There was a predominance of males involved in cases (12 male, 2 female). Eleven of the cases involved the branded product NRG-1. The age range of patients involved was 18–44 yrs (median 28). In 8 (57%) cases the patient ingested the product. In 5 cases it was insufflated. One case involved injection. The dose involved was frequently not reported but in two cases it was stated at 4 g and 5 g. All patients reported to NPIS were symptomatic. Symptoms reported were: tachycardia (9); agitation (8); anxiety (4); psychosis/hallucinations (3); paranoia (3); hypertension (2); dystonic movements (2); slurred speech (2); sweating (2); sluggishness (2); raised CK (2); ataxia (1); confu-

sion (1); nystagmus (1); peripheral vasoconstriction (1). **Conclusion:** Cases of alleged naphyrone exposure reported to the NPIS frequently produced symptoms. Tachycardia and agitation were the most common symptoms reported. In cases of ingestion of branded products caution must be used as the ingredients involved are not certain. Improved laboratory assays would aid identification and help determine the level of harm associated with new drugs of abuse. **Reference:** 1. <http://www.homeoffice.gov.uk/publications/drugs/acmd1/naphyrone-report?view=Binary> [accessed 18 Feb 2012].

#### 97. Drug Poisoning in Moroccan Children

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**Objective:** The present retrospective study aimed to describe the epidemiology, clinical features and outcome of all cases of drug poisoning occurring in children under 15 years and reported to the Moroccan Poison Control Centre from January 1981 to December 2009. **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”. Analysis of data used the EPI INFO 6 program. Univariate analysis was conducted to identify factors associated with severe poisoning (grade 3 and grade 4). **Results:** In our study, we collected 245 cases of drug poisoning in children. The mean age of victims was  $6.51 \pm 4.98$  years, while sex ratio was 2.8 in favour of male sex. Oral route was involved in 92.1% followed by inhalation in only 5.6% of the cases. Maajoune was the most commonly drug found (69.5%) followed by cannabis. Almost 60% of the cases occurred in children over 10 years. Accidental exposures represented 62.3% of the cases, followed by addition in 16%. According to the PSS, 52.7% of patients were classified in grade 2 and only 5.4% in grade 3. The clinical signs were represented by cardiovascular (49%) followed by neurological signs (23%). Three deaths were reported; two were due to cannabis and one due to maajoune. **Conclusion:** Drug poisoning is relatively frequent in Moroccan children, thus epidemiological investigations are required to better assess the impact of such poisoning.

#### 98. Energy Drinks: Health Risks and Toxicity Profile

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**Objective:** To describe the epidemiology and toxicity of caffeinated energy drink exposures in Australia. Caffeinated energy drinks have become popular due to their purported benefits of stamina and increased alertness. Increasingly, toxicity from caffeine overdose is being reported to hospitals and poisons centres. **Methods:** Retrospective review of calls to the Australian Poisons Information Centre Network over 7 years to 2010. A specific search strategy was used to extract calls from the database and individually reviewed. The main outcome measures were type of exposure,

co-ingestants, symptoms reported, age, gender, dose, brand of drink, and hospitalisation status. *Results:* The preliminary results from calls to the largest poisons centre in Sydney (handles approximately half of the national calls) revealed 297 exposures to energy drinks with an increasing trend from 12 in 2004 to 65 in 2010. In the 217 recreational exposures, the median age was 17 years (IQR: 15–21; range: 11–60) and 57% were male. Ninety-four cases co-ingested other substances, predominantly alcohol (n = 50) or other caffeinated products (n = 44). The number of drinks consumed in one session varied greatly (median: 5 units; IQR: 3–8; range: 1–80). Symptoms were common (87%), the most commonly reported being palpitations, agitation, tremor and gastrointestinal upset. Twenty-one cases had signs of serious cardiac or neurological toxicity including hallucinations, seizures, arrhythmias or cardiac ischaemia. At least 128 cases (57 with no co-ingestants) required hospitalisation. *Conclusion:* The increasing number of people, particularly adolescents, experiencing toxicity from energy drink consumption warrants review and regulation of the labelling and sales of these drinks. Adolescent education and increasing awareness in the community is paramount to addressing the hazards from energy drinks.

#### 99. Feasibility of the European Electronic Database and Protocols for Cross-Border Distribution (Mutual Exchange) of Radiation Antidotes Using Poison Centres and Radiation Emergency Assistance Centres Networks

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*Objective:* Proliferation of nuclear technology is associated with a certain risk of radiation/nuclear accidents (RNA), so the probability of contamination of the population with radionuclides requires attention. The experience from the event at Fukushima Dai-ichi nuclear power plant (NPP) can be used to improve the national and European systems of preparedness to RNA. *Methods:* Available information on the RNA at Fukushima NPP was analyzed. Computer simulation models of contamination of the area in the vicinity of Dukovany NPP (Central Europe) were used. National radiation antidote stockpile was estimated. *Results:* Total discharge amounts of I-131 and Cs-137 from the reactors of Fukushima NPP are known, but no accurate data are available on Sr-90, Pu-241, Te-127m. Screening surveys for residents revealed 102 people with external contamination. There are no data on patients with internal contamination requiring treatment. The 20-km zone around Dukovany NPP has a population of 95,805 people. The national radiation antidote stockpile is limited and anticipated to be sufficient for treatment of 10–20 patients for 1–2 weeks. The problems of national radiation antidote stockpiling are: rare use in daily life (chelation therapy of poisonings), high cost, rapid expiration, lack of national registration, difficult production planning. On the basis of information on RNA occurring worldwide, it is difficult to predict the potential number of people who would be contaminated with radionuclides. As Fukushima NPP experience indicates, it is likely to be several tens/hundreds rather than thousands. Even more difficult is to predict the number of people with internal contamination, because many variables

depend on the scenario of the event. Currently there are no prerequisites for confidence that national antidote stockpiles will be sufficient in any event. In the “Fukushima-like” cases the feasibility of antidote treatment remains unclear. In other cases (malicious use of radionuclides in terrorist acts) the feasibility can be unconditional. *Conclusion:* The need to supply sufficient quantity and spectrum of antidotes “on the spot” during the first days is confronted with primary uncertainty about the scenario of event. The European electronic database and protocols of cross-border antidotes distribution (mutual exchange) using the Poison Centres (Radiation Emergency Assistance Centres) networks can help cope with the problem.

#### 100. International Co-operation in Treatment of Suicidal Thallium Intoxication

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*Objective:* Intoxication with thallium belongs to the family of rare poisonings because its use has been banned in most countries due to extreme toxicity. The availability of the antidote and facilities for toxicological analysis may therefore be limited. Cross-border management of severe thallium poisoning enabled us to treat a severely poisoned patient. *Case report:* A 24-year-old student of chemistry, 70 kg body weight, ingested 100 mg of thallium bromide. He developed two episodes of unconsciousness and was admitted to the hospital, complaining of paraesthesiae in the limbs and progressive severe pain. Toxic encephalopathy with delirium was found. Treatment with Prussian blue, Fe<sub>4</sub>[Fe(CN)<sub>6</sub>]<sub>3</sub>, was started<sup>1</sup>, however the need emerged to contact a toxicological information center in a neighboring country, as the home country did not have sufficient stock of the antidote nor laboratory facilities to measure thallium in biological samples. As urine thallium measured during the antidote treatment reached 1460 micrograms/L (N less than 5 micrograms/L), 10 packages of antidote were supplied. The treatment lasted for 30 days (last urine level was 107 micrograms/L), and included charcoal, lactulose, analgesics (tramadol, trimecaine, metamizol), neuroleptics and tianeptine for psychotic symptomatology. Cheilitis and alopecia areata were present; in addition a partial atrophy of the left optic nerve, without vision loss, was found. Toxic polyneuropathy was the only residual feature at the time of transfer to the psychiatric department on the 30th day. *Conclusion:* Cross-border co-operation enabled timely antidote administration and measurements of thallium elimination in the case of a suicide attempt with a toxic dose of thallium (lethal dose is about 10 mg/kg body weight). Such a dose may lead to long-term consequences, especially polyneuropathy and vision loss.<sup>2</sup> Co-operation among several poison centers occurred thanks to personal contacts; however a system with a protocol and conditions for international antidote supply should be formed in order to manage rare poisonings adequately and in a timely manner. *References:* 1. Hoffmann RS. Thallium toxicity and the role of Prussian Blue in therapy. *Toxicol Rev* 2003; 22:29–40. 2. Pelclová D, Urban P, Ridzon P, et al. Two-year follow-up of two patients after severe thallium intoxication. *Hum Exp Toxicol* 2009; 28:263–72. *Acknowledgements:* MSM0021620807.

#### 101. Analysis of Seven Years of Activity in the Supply of Antidotes Provided by the Antidotes Reference Center of Emilia Romagna Region (Italy)

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*Objective:* Antidotes are life-saving drugs normally taken in a variable lapse of time ranging from a few minutes to four/six hours after the patient's poisoning. In order to promote a suitable resource allocation and appropriate treatments for intoxicated patients the Regional Health Services have identified a regional center for the management of antidotes;<sup>1</sup> the aim was to organize a network system to ensure optimal management of intoxicated patients. The Pharmacy Department of the University Hospital of Ferrara (AOUFE) has been appointed Regional Centre of Reference for the supply of antidotes, supplying an Italian region of 4,432,439 inhabitants. The study aimed at analyzing the transfer of antidotes carried out by the antidotes regional center from 01/01/2005 to 30/11/2011. *Methods:* The analysis was performed on requests for emergency supply of antidotes received by the Reference Center in 7 years. All demands from external services have been classified according to different criteria: a) geographical, according to the geographical area of the requesting organization, this has been divided into provincial, regional and extra-regional; b) type of antidote, according to the active principle requested. *Results:* 70 demands for antidote supplies coming from provincial, regional and extra-regional hospitals were registered. More precisely: 21.4% (15/70) from hospitals located in the province of Ferrara, 67.1% (47/70) from hospitals located in the Region Emilia-Romagna, 11.5% (8/70) from centers outside the region. Overall, the type of antidote was as follows: viper venom-specific antibodies 27 requests (38.7% of antidotes provided), pralidoxime 8 (11.5%), fomepizole 7 (10%), N-acetylcysteine 5 (7.2%), digoxin-specific antibodies 4 (5.7%), flumazenil 4 (5.7%), glucagon 3 (4.3%), dantrolene 3 (4.3%), ethyl alcohol one (1.4%), and one each of methylene blue, dimercaprol, sodium nitroprusside, penicillamine, procainamide, propranolol, protamine, and trometamol. *Conclusion:* The repeated request for viper venom-specific antibodies suggests a possible reallocation of this antidote in the territory, to facilitate more rapid availability. The request for flumazenil and acetylcysteine underline the absence of cheap antidotes for relatively frequent poisonings, such as paracetamol and benzodiazepines, in some hospitals. *Reference:* 1. Regione Emilia Romagna. Statement of Italian General Direction of Health ASS/DIR/04/752; 13/1/2004.

#### 102. Antidote Stocking in Acute Hospitals in the United Kingdom

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**Objective:** To survey the availability of antidotes in acute hospitals in the United Kingdom following the publication of joint College of Emergency Medicine and National Poisons Information Service guidelines on antidote stocking in 2008. **Methods:** A questionnaire was sent to the Chief Pharmacist in 224 hospitals with emergency departments in the UK in July 2010 requesting information on the availability of 28 antidotes categorised in 3 groups: available immediately (category A), available within 1 hour (category B) and available supra-regionally (category C). **Results:** Completed questionnaires were received from 196 (87.5%) of the 224 hospitals by the survey completion date of 31st January 2011. In the category A list of antidotes, commonly used antidotes such as acetylcysteine, activated charcoal, naloxone, flumazenil were available for immediate use in more than 90% of hospitals surveyed but the availability of cyanide antidotes was much lower. Dicobalt edetate, currently recommended as the antidote of choice for severe confirmed cyanide poisoning, was available immediately in 144 (74%) and was not stocked in 29 (15%) hospitals. Hydroxocobalamin, sodium nitrite and sodium thiosulphate were available for immediate use in 21%, 57% and 66% of hospitals respectively. In the category B list, dantrolene, desferrioxamine and phytomenadione (vitamin K) were available for use within 1 hour in more than 90% of hospitals but there was poor availability of cyproheptadine (45%), viper venom antiserum (45%), pralidoxime (30%) and antidotes used for the treatment of toxic alcohol poisoning, with intravenous ethanol being available within 1 hour in 72%, oral ethanol in 28% and fomepizole in 18% of hospitals. Antidotes which are rarely used and recommended for supra-regional stocking were stocked in few hospitals, ranging from 4% for DMSA and DMPS, 20% for botulinum antitoxin and 25% for sodium calcium edetate. **Conclusion:** Commonly indicated antidotes are widely available but there is inconsistent stocking of less commonly used antidotes, for example those used to treat poisoning with organophosphorus insecticides, cyanide and toxic alcohols. This is of concern because these agents are frequently associated with severe morbidity and mortality and the timely use of an appropriate antidote may be life-saving in these situations.

### 103. Fire Smoke Inhalation and Cardiac Disorders – Efficacy of Hydroxocobalamin: Final Results

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**Objective:** Traditionally, the diagnosis of cyanide intoxication after smoke inhalation is made on the following clinical signs: coma or altered neurological status, cardiac arrest, state of shock. In addition to these classic clinical signs, there are also cardiovascular manifestations which are indicative of poisoning. **Methods:** An open, retrospective, multicentre (Paris, Besançon, Dôle, Montbéliard, Vesoul) study was conducted from 1995 to 2011 from a systematic review of 176 medical observations records, from mobile emergency and resuscitation services. Only patients with inhalation of fire smoke treated with hydroxocobalamin were included. The analysis involved the electrocardiographic trace recorded on the arrival of the medical team at the scene

**Table 1.** Cardiac disorders in cyanide intoxication after smoke inhalation.

Cardiac disorder	Type	Number
Cardiorespiratory arrest	Asystole	58
	Ventricular fibrillation	3
Repolarization disorders	Myocardial ischemia	5
	Subendocardic lesion	7
Conduction disorders	Intracardiac	5
Heart rhythm disorders	Supraventricular tachycardia	64
	Ventricular tachycardia	1
	Auricular extra-systoles	1
	<b>Total</b>	<b>144</b>

of fire and continuous electrocardioscope monitoring data. **Results:** Of the 176 patients suspected of acute hydrogen cyanide poisoning, 144 exhibited cardiac disorders confirmed on the initial electrocardioscope or electrocardiographic trace (Table 1). **Conclusion:** In this study, the cardiac disorders found were principally cardiac arrests, repolarization and rhythm disorders. These results show that early administration of the antidote appears to be an essential prognostic factor in cases of cardiorespiratory arrest. In the absence of the possibility of a rapid assay of blood cyanides, treatment must be administered presumptively on the basis of the patient's history (enclosed environment, fire), the clinical signs observed (disorders of consciousness, hypotension, cardiorespiratory arrest) and laboratory findings (disorders on the electrocardiogram, raised lactate levels). In the event of manifest cardiorespiratory arrest or circulatory insufficiency, the dose of hydroxocobalamin must be increased or even repeated in the absence of a rapid response.

### 104. Acute Cyanide Poisoning in Prisons: Two Case Reports

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**Objective:** The number of suicides in prisons has been increasing in France (10/10,000 prisoners in 1980, 23.3/10,000 prisoners in 2003). Hanging remains the most frequent method (92% of cases), and suicide by medicinal products the second (3.5% of cases), but mattress fires with fire smoke inhalation account for some attempted suicides. **Case series:** Two cases of patients in Besançon prison who suffered fire smoke poisoning after deliberately setting fire to a mattress in their cells. Case no 1: This 23-year old male patient was exposed to fire smoke for 30 minutes. He was found in a state of cardio-respiratory arrest at 10:24 am. Cardiac activity was observed after external cardiac massage and oxygen therapy using a mask. The administration of hydroxocobalamin (5 g IV) was started at 10:57 am. The initial tracing of the ECG showed a current corresponding to a sub-endocardial lesion. This was subsequently confirmed by assays of blood levels of cyanide ([CN] = 6.12 mg/L) and lactates (8.42 mmol/L), in samples taken before the administration of hydroxocobalamin when the SMUR (Service Mobile d'Urgence et Reanimation) took charge of the patient. A second administration of hydroxocobalamin was given at the

hospital. Case no 2: A 30-year old man was exposed to fire smoke after deliberately setting fire to his mattress. The first assessment by the emergency medical services revealed tachycardia of 140 bpm and a blood pressure of 110/70 mm Hg. At the hospital, his admission examination found persistent tachycardia of 140 bpm, blood pressure of 80/44 mm Hg, and a carboxyhaemoglobin level of 41%; the assay of blood cyanides revealed a level of 2.5 mg/L (= LC<sub>50</sub>) and a lactataemia of 6.11 mmol/L. It was finally decided to administer hydroxocobalamin (5 g) at 11:27 a.m., i.e. two hours after the poisoning. **Conclusion:** Hydroxocobalamin, which has been in use for more than 10 years, remains the only effective antidote following acute massive cyanide poisoning.

### 105. Acute Liver Failure in a Term Neonate with Repeated Paracetamol Ingestion and Suspected Metabolic Disease: Case Report

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**Objective:** To report a severe liver injury in a neonate with suspected metabolic disease associated with repeated paracetamol ingestion, and treated with IV N-acetylcysteine (NAC). **Case report:** A 26-day-old male child (birth weight: 3,160 g) was referred to our neonatal intensive care unit (ICU) with a history of irritability, a refusal to feed (4 days), vomiting (1 day) and low fever (37.7°C), as well as intestinal bleeding, jaundice, signs of shock and slight liver enlargement. The main laboratory findings on admission were incoagulable blood (incoagulable INR, TT and aPTT), metabolic acidosis (pH = 7.21, bicarbonate = 7.1 mEq/L, lactate = 4.3 mmol/L), hypoglycemia (18 mg/dL), increased serum aminotransferase activity (AST = 4,039 IU/L, ALT = 1,087 IU/L), and bilirubin (9.6 mg/dL; direct = 6.18 mg/dL). The child had been exclusively breastfed and had received paracetamol (10 mg/kg every 4 h, for 3 days; total dose ~180 mg/kg) that was interrupted ~24 h before admission. The serum paracetamol concentration ~48 h after the last dose was 77 µg/mL. Subsequent metabolic investigation detected elevated long-chain acylcarnitines in the first sample, (day 2; tandem mass-spectrometry), but not in the second sample (day 30), suggestive, but not conclusive of a palmitoyltransferase type 2 (CPT2D) or carnitine-acylcarnitine translocase (CATD) deficiency. Apart from supportive measures, a 21 h IV NAC protocol (total dose, 300 mg/kg) was started, followed by continuous IV NAC (6.25 mg/kg/h). During follow-up AST and ALT decreased progressively, blood coagulation parameters improved and NAC was stopped on day 9 (INR = 1.4; AST = 94 IU/L, ALT = 79 IU/L). No adverse effects were observed during NAC use. The patient was discharged on day 34. **Conclusion:** Metabolic attacks associated with infantile CPT2D and CATD are usually triggered by fasting or febrile illness, with the clinical picture involving episodes of acute liver failure, hypoglycemia, metabolic acidosis and transient hepatomegaly. However, since experimental studies have shown that high doses of paracetamol may also significantly inhibit fatty acid oxidation, it is difficult to conclude whether the acute liver failure observed here was caused exclusively by paracetamol or by repeated paracetamol ingestion in conjunction with an inborn defect in β-oxidation enzymes (most likely possibility).

### 106. Review of Poison Center Practice: Recommendations and the Variables that Influence Practice When the Acetaminophen Nomogram is not Applicable

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**Objective:** Risk stratification for acetaminophen (APAP) exposures that do not meet criteria for application of the treatment nomogram is challenging and strong evidence based guidelines are lacking. We examine Poison Centre (PCC) recommendations provided in APAP exposures when the nomogram is inapplicable and the variables influencing recommendations to identify practice variability and aid future risk stratification. **Methods:** The PCC database was queried for APAP exposures from 1/1/2008–12/1/2010 when physician consultation was offered. A convenience sample of 471 of the resultant 1406 was analyzed. Exclusion criteria were: Use of the nomogram (n = 203), Missing data (n = 45), Duplicates (n = 4), Miscoding (n = 11). Variables studied included patient demographics, ingestion history, laboratories and recommendation regarding NAC, in the 208 remaining cases. **Results:** Mean age 35.5 years, 38% male, 37% chronic ingestions, 63% uncertain, 91% ingested a single APAP product (35% opiate formulations), 57% co-ingestions, 8% chronic alcohol abuse, 12% reported a co-morbidity (hepatitis, shock liver, etc), 51% [APAP] < 10 µg/mL (66.2 µmol/L), mean [APAP] 52.9 µg/mL (349.5 µmol/L), [AST] and [ALT] normal in 29.3% and for the remainder, mean [AST] 825.61 U/L and [ALT] 694.36 U/L. One hundred and twenty-two of 208 total (59%) recommended NAC (group 1), 38 (18%) recommended repeat aminotransferases to aid decision making (group 2), and 48 (23%) recommended no NAC indicated (group 3). Overall, 58% received NAC. All cases ultimately fulfilling Kings College Criteria had NAC initially recommended. There were 7 cases of noncompliance with no significant predictors. When adjusting for sex, chronicity, co-morbidity, [APAP], [AST], and [ALT] only history of a co-morbidity (OR 0.86, p < 0.05, 95% CI 0.012–0.627) and [APAP] (OR 1.03 per unit increase, p < 0.05, 95% CI 1.006–1.055) were significant predictors of requesting repeat aminotransferases to aid decision making (recommendation group 2). The only significant predictor of liver transplant (n = 2) and/or death (n = 10) was ingestion of multiple APAP-containing formulations (OR 6.5, 95% CI 1.7–24.4, p < 0.05). **Conclusion:** When the APAP nomogram is inapplicable consultants are reluctant to provide definitive recommendations based on a single [APAP] and [AST] especially in patients without comorbidities and with elevated [APAP]. PCC recommendations are not always followed. Future research may define the variables that influence practice and noncompliance with recommendations and aid in developing consistent recommendations.

### 107. The TOXBASE® New Product and Unusual Cases Reporting Scheme – Paracetamol

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**Objective:** To describe unusual paracetamol exposures reported to The National Poisons Information

Service Edinburgh Unit (NPIS). NPIS is aware that on some occasions patients present with what appears to be a non-toxic concentration of paracetamol (below treatment line) but that the subsequent clinical course may suggest problems with the nomograms currently used. To address this issue NPIS collects reports of unusual poisonings through the UK national on-line toxicology database TOXBASE®. **Methods:** Unusual case reports are submitted electronically by users via an on-line form. Reported cases are collated and analysed by NPIS. **Results:** Between August 2001 and October 2011 49 cases of paracetamol ingestion were reported. Twenty-four (49%) were symptomatic, 17 had no symptoms and in 8 cases symptoms were unknown. The age range of patients was 8 months to 65 years (median 20). The dose ingested ranged from 500 – 40,000 mg (median 10,000 mg). The majority of reports were unremarkable. Forty-four cases may have been unusual in the way the tablets were taken, or in patient history, but not in clinical outcome. Five cases reported patients who came to harm or developed hepatic dysfunction despite initially not being thought to be at risk. Of the 5 reports received, one patient is known to have died and one was referred to a Liver Unit. This patient was lost to follow up. The other 3 cases recovered fully with treatment. Four cases may have involved mistakes in the timing of ingestions, 2 patients may have had undisclosed or unidentified risk factors, 2 cases may have taken drugs affecting gastric emptying. In one case the patient may have taken an earlier undisclosed overdose. **Conclusion:** NPIS receives very few on-line reports indicating unusual toxicity profiles from paracetamol. The small number of reports received indicates common themes that other NPIS systems also detect. Adequate risk assessment, ensuring timing of overdose and no previous ingestions, and awareness of accurate dose timing of single ingestions are key to appropriate treatment.

### 108. Overestimation of N-Acetylcysteine Treatment in Acetaminophen Overdose According to Ingested Dose

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**Objective:** N-acetylcysteine (NAC) is an antidote used in acetaminophen overdose. The indication for NAC treatment is toxic levels of serum acetaminophen according to the acetaminophen treatment nomogram. However, in some toxicology units NAC treatment is decided according to the ingested dose. The objective of the current study was to find out the percentage of patients who were treated with NAC unnecessarily. **Methods:** This was a one-year prospective study including patients admitted to a toxicology unit in a referral hospital in the province of Mazandaran, Sari, northern Iran due to acetaminophen overdose who required NAC treatment according to dose of ingestion ( $\geq 6.5$  g in adult or  $> 150$  mg/kg in children). Serum acetaminophen was measured after 4 hours post-ingestion. Using the acetaminophen treatment nomogram patients who required antidote therapy due to risk of hepatotoxicity were identified. Data were presented as mean  $\pm$  SD. **Results:** Over a one year period 39 patients, 13 male and 26 female with mean age of 22.77  $\pm$  4.93 admitted to the toxicology unit following acetaminophen

overdose required NAC treatment according to dose of ingestion. The mean amount of acetaminophen ingested was 8.99  $\pm$  5.59 g. All cases of overdose received the Prescott intravenous NAC infusion protocol. The mean serum acetaminophen level and time of measurement were 27.79  $\pm$  30.37 mg/L and 6.16  $\pm$  4.95 hours, respectively. No patient developed liver function test derangement. According to the acetaminophen treatment nomogram only two cases required NAC treatment and in 37 subjects the antidote treatment was overestimated. Fourteen cases developed some degree of NAC adverse reaction. **Conclusion:** Acetaminophen overdose is not a common toxicity in Iran, particularly in Northern Iran. Using the dose of ingestion as a diagnostic tool for antidote therapy in acetaminophen overdose results in overestimation of treatment required and imposes the risk of NAC adverse reactions in patients and longer hospitalization.

### 109. Two Cases of Bactrian Pharmacokinetics in Large Acetaminophen and Diphenhydramine Co-Intestions: Management Implications

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**Objective:** Delayed peak acetaminophen concentrations may occur following massive overdose and with co-ingestants that slow intestinal motility, yet no formal recommendations address alternative N-acetylcysteine (NAC) regimens. We report two cases of bactrian (“double peak”) acetaminophen pharmacokinetics and describe differing management strategies. **Case series:** Case One: A 25 year-old man was found unresponsive on St Patrick’s Day. Emergency department (ED) initial vital signs were: BP 131/79 mmHg; HR 109 beats/min; RR 18 breaths/min; T 37.6°C; SpO<sub>2</sub> 97% on 2L via nasal canula. His physical examination being unremarkable, he was observed for 8 hours for presumed ethanol intoxication. When he failed to improve, laboratory studies showed: lactate 7 mmol/L; acetaminophen 447 micrograms/mL; AST 166 IU/L; ALT 184 IU/L; and INR 1.48. A 21-hour NAC infusion was started. Serial acetaminophen concentrations revealed an initial decline to 275 micrograms/mL after 4-hours with a second peak of 384 micrograms/mL, 6.5 hours later. Repeat ingestion was impossible as he remained unconscious. After 21-hours of NAC, acetaminophen concentration was 163 micrograms/mL, and NAC was continued at 12.5 mg/kg/hr IV until the acetaminophen concentration was undetectable, followed by 6.25 mg/kg/hr IV until his laboratories normalized. AST peaked at 10,726 IU/L on day 1. INR peaked at  $> 10$  on day 2. Mental status, liver and renal function normalized by 2.5 weeks. He reported ingesting three bottles of acetaminophen with diphenhydramine. Case Two: A 45 year-old woman was found unresponsive with an empty bottle of acetaminophen/diphenhydramine. ED vital signs were: BP 154/84 mmHg; HR 120 beats/min; RR 35 breaths/min; T 34.3°C; SpO<sub>2</sub>, 100% on room air. Physical examination was unremarkable. Initial acetaminophen concentration was 533 micrograms/mL with normal transaminases. Twenty-one-hour NAC regimen was started and acetaminophen decreased to 196 micrograms/mL at 12-hours but increased to 208 micrograms/mL at approximately 24 hours. As she remained unresponsive repeat ingestion was impossible. NAC dosing was never increased. By 30 hours, her acetaminophen concentration was 87.9 micrograms/mL. Her transaminases remained normal throughout, on

NAC (6.25 mg/kg/hr IV) until her acetaminophen was undetectable. *Conclusion:* Since delayed or bactrian pharmacokinetics can occur following large ingestions or co-ingestions, serial acetaminophen concentrations may be indicated. No consensus exists regarding the optimal NAC regimen in these cases.

### 110. Clinical Review of Intoxicated Patients with Acetaminophen Extended Release Preparations

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*Objective:* The Rumack-Matthew nomogram cannot be applied for managing acetaminophen (AAP) overdose with extended release (ER) preparations. This study is to analyze the clinical characteristics of the AAP ER overdose in order to develop treatment recommendations. *Methods:* We reviewed retrospectively the medical records of patients presenting to the emergency department with AAP overdose from Jan 2008 to Dec 2010. Patients ingesting extended release preparations of AAP were included. Their blood AAP concentrations were measured at 4 hours after ingestion and one additional acetaminophen level was measured 4 hours after the first sampling. The clinical variables related to poisoning were analyzed. *Results:* During a 3-year period, 20 patients with AAP ER overdose were identified among 108 AAP overdose patients. The estimated amount of ingestion was 167.5 mg/kg. Gastric lavage, activated charcoal, and N-acetyl cysteine (NAC) treatment were performed 10, 14, and 11 patients, respectively. Hepatotoxicity was diagnosed in only one patient who was treated successfully with NAC. One person had a level taken on arrival in hospital 11 hours after ingestion and a second level 3 hours later (14 hours after ingestion by mistake); the blood AAP concentration was increased 3 hours after the first test. Nineteen persons had levels at 4 hours after ingestion and then 8 hours after ingestion and the levels at 8 hours had decreased from the 4 hour level and were then below the "200" line. *Conclusion:* This study suggests that the blood AAP concentration could be increased in delayed fashion. Therefore, multiple blood sampling for AAP concentration may be needed in the setting of extended release overdose.

### 111. Elevated Acetaminophen-Cysteine Adducts Facilitate Diagnosis of Acetaminophen Toxicity in a Case of Unexplained Acute Liver Failure

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*Objective:* Acetaminophen-cysteine adducts (APAP-CYS) are a biomarker of acetaminophen exposure and are formed when the oxidative metabolite of acetaminophen binds to cysteine residues in hepatic proteins. APAP-CYS adducts have been shown to become elevated in cases of liver failure following acute acetaminophen overdose and in patients who develop liver injury following repeated excessive

**Table 1.** APAP-CYSTEINE protein adduct levels in the patient\*, in therapeutic acetaminophen dosing\*\* and in acetaminophen overdose and toxicity<sup>1\*\*\*</sup>.

Sample Number (consecutive samples)	Sample Type	[APAP-CYS] nmol/mL in our patient*	[APAP-CYS] levels with therapeutic dosing (mean (SD) peak levels) for non drinkers**	[APAP-CYS] levels in apap-overdose and toxicity***
001	Serum	10.130*	0.4 (SD 0.20) nmol/mL**	0.10–27.3 nmol/mL***
002	Serum	6.206*	--therapeutic dosing--	--OD & toxicity--
003	Serum	4.901*	-----	-----

dosing of acetaminophen. We compared APAP-CYS levels from a patient with acute liver failure, with suspicion that acetaminophen overdose was the cause of her liver failure, to APAP-CYS levels previously reported in acetaminophen overdose, excessive chronic dosing and in therapeutic acetaminophen administration, and discuss the use of APAP-CYS levels in facilitating diagnosis and treatment of patients with acute liver failure of uncertain etiology. *Case report:* A 26 year-old female with history of unexplained, severe, hepatitis presented with a second episode of severe hepatitis including coagulopathy and transaminases > 10,000 U/L. The patient reported ingesting only, "a couple" of acetaminophen several days prior to her presentation. Acetaminophen concentrations of 14 micrograms/mL at presentation aroused suspicion that acetaminophen may have caused the patient's liver failure although she adamantly denied overdose. APAP-CYS adducts measured from serum obtained four days after presentation and in two consecutive serum samples are reported alongside previously reported APAP-CYS levels<sup>1</sup> (Table 1). *Conclusion:* The patient's APAP-CYS adduct levels are consistent with acute liver injury following acetaminophen overdose or liver injury from repeated excessive dosing of acetaminophen. *Reference:* 1. Heard KJ, Green JL, James LP, et al. Acetaminophen-cysteine adducts during therapeutic dosing and following overdose. BMC Gastroenterol 2011; 11:20.

### 112. Acute Liver Toxic Damage by Hepatotoxic Substances and New Treatment Method

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*Objective:* Administration of carbon tetrachloride to laboratory animals is a widely used model to study mechanisms of hepatic toxic injury. It leads to hepatocyte injury that is characterized by centrilobular necrosis. Administration of carbon tetrachloride, *Amanita phalloides*, hepatotoxic medications and other hepatotoxic agents determines liver injury, inflammation and oxidative stress; molecular mechanisms of damage are only partially understood. The authors present an original method of treatment for toxically damaged liver by antihepatocytotoxic serum and restoration of toxically damaged liver's lost function. *Methods:* 160 white Wister line rats were selected as experimental animals. They were divided into 4 groups. The animals of group I (n = 40) were used for the modelling of acute liver injury by injection of the hepatocytotoxic agent CCl<sub>4</sub> "carbon tetrachloride". In animals of group II (n = 40) 60% liver resection was performed. Group III (n = 40) animals served as hepatocyte donors (progenitor hepatocytes) for antihepatocytotoxic serum. Group IV (n = 40) animals

were used as control group. On the third day after liver toxic damage and hepatocellular injury by 70% liver resection, we started treatment with antihepatocytotoxic serum which was made from progenitor hepatocytes which were on reparative regeneration activity, and we administrated it into the abdominal cavity. Quantitative analysis of collagen in Sirius Red-stained liver sections was performed by morphometric analysis. Briefly, liver sections were stained with Sirius Red, and slides were computer analyzed to calculate the percentage of collagen in total liver tissue area using Scion Image Beta 4.0. *Results:* The performed studies showed that antihepatocytotoxic serum prevents liver-cell necrosis, promotes reparative regeneration process in toxically damaged liver cells, and helps in restoration of organ's function. Micro morphological studies have shown structure and function restoration in hepatocytes organelles (mitochondria and endoplasmic reticulum), normalization of morphological picture and biochemical measurements. *Conclusion:* The performed research has shown that antihepatocytotoxic serum promotes hepatocyte reparative regeneration and helps toxically damaged liver in function restoration.

### 113. Mining for Mechanisms of Glycol-Induced Renal Toxicity in Order to Dig Up New Treatments

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*Objective:* Ethylene glycol (EG) and diethylene glycol (DEG) poisonings can produce an acute renal failure that, in many cases, is treatable only with long-term hemodialysis. In the case of EG exposures, renal accumulation of calcium oxalate monohydrate (COM) crystals is responsible for the associated kidney injury. In situations where metabolic inhibitor therapy (fomepizole or ethanol) is delayed because of late admissions to the hospital or problems in recognizing the diagnosis of EG toxicity, long-term kidney injury is common. The development of a pharmacological approach to reduce the toxicity from COM accumulation in the kidney would be valuable to decrease the renal toxicity not only in late treated cases of EG poisoning, but also in other hyperoxaluric diseases such as primary hyperoxaluria and kidney stone formation. DEG has produced numerous mass poisonings worldwide, primarily because it has been mistakenly used as a solvent in drug formulations. Limited information exists regarding the mechanism of renal toxicity of DEG, so there are no treatment measures except for hemodialysis which can be limited in mass poisonings. *EG Discussion:* Our *in vitro* studies have shown that aluminum citrate blocks the toxicity of COM on human proximal tubule cells by preventing COM attachment and internalization. The ability to minimize COM binding and cytotoxicity represents a unique molecular target, not reproduced by citrate salts already used for stone

therapy. Thus, studies have recently evaluated the efficacy and mechanism of action of aluminum citrate in a rat model of EG poisoning. Wistar rats were treated with either control (water at time 0), EG (6 g/kg, gavaged at time 0), or EG + aluminum citrate (0.2 mmol/kg, given IV at 2, 6, and then every 6 h to 72 h, with saline for controls at the same times). BUN and plasma creatinine levels were increased by EG treatment and this effect was blocked by the co-treatment with aluminum citrate. Urinary excretion of insoluble oxalate and insoluble calcium was significantly increased in EG-treated rats by aluminum citrate, while soluble calcium and oxalate were reduced by aluminum citrate, indicating enhanced excretion of calcium oxalate as crystalline material. The amount of COM crystals in kidney tissues was markedly reduced by aluminum citrate. These effects occurred even though the EG-treated animals were acidotic and were continuing to produce oxalate throughout the study. These results suggest that aluminum citrate could decrease COM-induced renal injury by decreasing COM retention in the kidney, thus enhancing the excretion of both calcium and oxalate. *DEG Discussion:* Recent studies have convincingly shown that a metabolite of DEG is responsible for producing the renal toxicity and attention has turned to understanding the mechanism of toxicity of the two major DEG metabolites, hydroxyethoxyacetic acid (HEAA) and diglycolic acid (DGA). *In vivo* and *in vitro* studies have been conducted to assess the respective roles of the two metabolites. Wistar rats were treated with toxic doses of DEG and blood and tissue samples were collected for 48 h for analysis of the concentration of DEG metabolites as well as markers of kidney toxicity. Also, human proximal tubule cells in culture were incubated with HEAA or DGA for up to 48 h and cytotoxicity was assessed using multiple measures of necrosis and of apoptosis. In the DEG-treated rats, blood HEAA levels peaked at 4.2 mmol/L, while blood DGA levels at 24 h were 0.04 mmol/L. However in the same animals, the kidney concentrations of DGA were 4–5 mmol/L, indicating a substantial concentrative uptake of DGA by kidney tissue. Kidney levels of both HEAA and DGA correlated strongly with increases in BUN and plasma creatinine. In the *in vitro* studies, HEAA at 100 mmol/L did not induce any necrosis or apoptosis, while DGA at > 25 mmol/L induced a marked degree of necrotic cell death, which was preceded by a depletion of ATP. Co-treatment with combined metabolites or with DEG did not exacerbate the toxicity produced by DGA. As such, further studies have examined the toxic mechanism of DGA and offer a therapeutic intervention in DEG poisoning. The central hypothesis is that DGA produces proximal tubule cell necrosis via a molecular mimicry mechanism leading to mitochondrial dysfunction. DGA is a four-carbon, dicarboxylic acid with structural similarity to many Krebs cycle intermediates that are utilized in cellular metabolism. Dicarboxylate transporters localized to proximal tubule cell membranes are responsible for concentrating these intermediates from the blood and tubular filtrate. Co-treatment with dicarboxylate transport inhibitors reduced the toxicity of DGA in cells, suggesting that kidney cell uptake of DGA was necessary for its toxicity. *Conclusions:* These studies suggest that a compound that works by the same mechanism as aluminum citrate, i.e. blocking COM retention by kidney cells, would be a useful treatment for the kidney damage produced by EG and might be useful in other diseases involving high levels of oxalate. These studies have also demonstrated for the first time that DGA is a key metabolite of DEG and that it is the likely toxic metabolite that produces the cortical necrosis observed in DEG poisonings. Further, pharmacologic strategies to diminish DGA uptake and/or intracellular toxicity may become useful in the therapy of DEG poisoning.

#### 114. Intravenous Fructose-1,6-Diphosphate Improves Survival and Blood Pressure in Propranolol-Poisoned Rodents

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*Background:* Fructose-1,6-diphosphate (FDP) is an intermediary metabolite in the glycolytic pathway created from glucose. Exogenously administered FDP potentially spares the consumption of 2ATP molecules required in its production from glucose, increasing net yield of ATP in anaerobic glycolysis. It reduces ischaemic tissue area in experimentally-induced cerebrovascular accident and myocardial infarction as well as improves haemodynamics post-cardiac bypass<sup>1</sup>. FDP also increases Na<sup>+</sup>/K<sup>+</sup>-ATPase activity and reduces toxicity in animal models of cardiac glycoside poisoning<sup>2</sup>. We hypothesised that exogenously administered FDP will improve survival in propranolol poisoning. *Methods:* Anesthetized, ventilated Wistar rats (n = 10 per group) were instrumented to record BP, heart rate (HR), cardiac output (CO) and QRS-duration. Propranolol was infused continually. When BP dropped to 50% of baseline, rats received one of 10%FDP125mg/kg or 10%FDP250mg/kg loading dose over 20 minutes followed by infusion 20 mg/kg/h. Controls received comparable volumes of 10% glucose for each treatment arm. Animals were observed until terminal bradycardia and hypotension resulted. Haemodynamics were compared at individual time points for FDP to Control by unpaired t-test or Mann-Whitney test as appropriate (p < 0.05). Survival was assessed using Kaplan-Meier survival analysis. *Results:* FDP-treated animals had significantly longer survival time than glucose-treated controls (median survival for both FDP doses was 140 mins v glucose 125 and 250 – 80 and 95 mins respectively, p < 0.0001). FDP250-treated animals showed a statistically significant increase in mean and systolic BP at t = 20, 35, 50, 65, 80 mins (P < 0.04). There was a trend to greater CO and HR and shorter QRS-duration with FDP250. FDP125 increased BP non-significantly with no difference in HR or QRS-duration from Control. *Conclusion:* FDP improved survival with a moderate dose-dependent improvement in haemodynamics in propranolol poisoning. Future research could examine the efficacy of FDP in other beta-blocker and calcium channel-blocker poisoning as well as in concert with other established inotropic therapies in toxin-induced cardiovascular collapse. *References:* 1. Riedel BJ, Gal J, Ellis G, et al. Myocardial protection using fructose-1,6-diphosphate during coronary artery bypass graft surgery: a randomized, placebo-controlled clinical trial. *Anesth Analg* 2004; 98:20–9. 2. Markov AK, Payment MF, Hume AS, et al. Fructose-1,6-diphosphate in the treatment of Oleander toxicity in dogs. *Vet Hum Toxicol* 1999; 41:9–15.

#### 115. The Role of Poisons Centres in Prevention of Poisonings

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*Objective:* To provide an outline of the development of varying strategies within the field of poisoning prevention. Besides giving advice regarding treatment of different acute intoxications in the emergency situation, activities aiming to prevent poisoning have been

considered important tasks for poisons centres since their establishment in the middle of the fifties until late sixties. *Methods:* PubMed was searched for relevant literature published 2000 – November 2011. Out of 24 articles, six were found that specifically discussed the role of poisons centres in prevention of poisoning. The WHO/IPCS directory of poisons centres was searched for web sites throughout the world and accessible web sites were visited (Americas region: 47, Europe: 36, Western Pacific Region: 4). Complementary information was obtained from colleagues in USA, Europe and Australia. *Results:* The first poisons centre was set up in the United States (Chicago 1953) and was shortly followed by a number of centres in the bigger European countries and Australia; the Swedish centre, established in 1960, actually being one of the first ones. The EAPCCT was founded in 1964 – six years after the AAPCC – during a meeting in Tours, France. Prevention of poisonings seems to have been a main topic of a congress for the first time in Utrecht 1978, where risks of injuries from household products and possible prevention of related poisoning accidents were discussed. Well worth noting is that prevention of poisoning was considered important enough to motivate the proclamation of the National Poison Prevention Week (a yearly event the third week in March) in the United States as early as 1962. The first traditional prophylactic measures taken were the preparation of information pamphlets regarding poisoning accidents in children – first aid, risky products, medicines and plants together with advice regarding safe handling of these agents. Fundamentally, the same (updated) pamphlets are used even today, but have been supplemented with various other information materials directed towards special target groups. Examples of such groups may be young people (drugs on the net!), elderly (safe medication) and tourists/immigrants (language barriers). The need for multilingual information from poisons centres seems to be neglected to some extent. Translation services in connection with the phone call to the centre are often available, but written information is commonly missing. To meet a serious problem in Sweden a new brochure about mushroom poisoning has been translated into 24 languages and can be downloaded from the web site of the Swedish Poisons Information Centre. Means for prevention of poisoning include vigilance (e.g. new phenomenon, new poisons, reappearance of old ones), lobbying (e.g. alerting authorities, and producers of chemical products or pharmaceuticals – legal actions, child-resistant closures, smaller packages, withdrawal from the market) and information to the general public as well as professionals. Modern communication techniques and social media have most certainly a potential to bring poisons centres' messages to general notice and should be used. Finally, do poisons centres activities prevent poisonings? The answer is not obvious. Two recent papers indicate that the prevention efforts are inadequate and need improvements.<sup>1,2</sup> An ambitious bilingual public education intervention concerning unintentional carbon monoxide poisoning was, however, successful.<sup>3</sup> Likewise was another randomized, controlled trial to evaluate a bilingual education program involving a videotape.<sup>4</sup> Probably, all education means must take possible barriers into consideration and also be repeated and reinforced for acceptable efficacy. However, as a comfort to disappointed poisons centres' staff, the length of hospital stay of poisoned patients has been shown to be significantly shortened if a poisons centre is consulted.<sup>5,6</sup> *Conclusion:* Prevention of poisoning has been a main task for poisons centres since their establishment more than fifty years ago, and there is no reason to abandon this. Instead, reasons accumulate for not sparing any effort to reduce harm from a wide

range of different toxic substances. The use of modern communication techniques and media provides hope for improved information efficacy, especially if obstacles like confusion of languages are taken into account. *References:* 1. Bond GR, Woodward RW, Ho M. The growing impact of pediatric pharmaceutical poisoning. *J Pediatr* 2012; 160:265–70. 2. Gutierrez J, Negron J, Garcia-Fragoso L. Parental practices for prevention of home poisoning in children 1–6 years of age. *J Community Health* 2011; 36:845–8. 3. Schwarz L, Martinez L, Louie J, et al. An evaluation of a carbon monoxide poisoning education program. *Health Promot Pract* 2010; 11:320–4. 4. Kelly NR, Huffman LC, Mendoza FS, et al. Effects of a videotape to increase use of poison control centers by low-income and Spanish-speaking families: a randomized, controlled trial. *Pediatrics* 2003; 111:21–6. 5. Bunn TL, Slavova S, Spiller HA, et al. The effect of poison control center consultation on accidental poisoning inpatient hospitalizations with preexisting medical conditions. *J Toxicol Environ Health A* 2008; 71:283–8. 6. Galvão TF, Silva MT, Silva CD, et al. Impact of a poison control center on the length of hospital stay of poisoned patients: retrospective cohort. *Sao Paulo Med J* 2011; 129:23–9.

#### 116. 50 Years Poison Information Service in Finland – What Has Changed?

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*Objective:* The Finnish Poison Information Centre (FPIC) serving the whole country was established in 1961 at Helsinki Children's Hospital as one of the first in Europe using the call-centre concept. At that time under 5 mortality in acute poisonings – excluding CO poisonings – was 15–20/year. The aim of this study was to look at some numerical indicators of the service during the 50 years. *Methods:* Statistics of the FPIC activities available and selected data from Statistics Finland were used. *Results:* In 5 years the total number of calls exceeded 1,000/year (21/100,000 population), in 19 years 10,000/year (209/100,000) and has since 2004 levelled off at around 40,000/year (730/100,000). The 1 millionth call was received in August 2011. The majority of calls related to exposures have concerned children, mostly children under 6 years of age (48–67% of calls related to exposures). Calls concerning children under 6 in relation to the age group population increased from 200/10,000 in 1981 to about 450/10,000 since 2003. Calls about adults varied from 24 to 32%. Calls from the public exceeded 50% on the third year of operation and continue to dominate (currently at 80% of all calls). Medicines have accounted yearly for 27–53% of total as cause of exposure while chemical products have accounted for 25–43%. Recommendation to use ipecac decreased from about 25% of yearly calls in the mid 1970s to below 5% at the beginning of the 1990s. Ipecac was substituted by recommendation of activated charcoal, which increased from 10% in 1970 to a peak of 40% in 1983, then decreasing to around 5% from 2005. In the 1970s the recommended place of treatment was home in about half of the calls, but increased to 80% in 1990s, and has remained at that level. The under 5 mortality – excluding CO poisonings – fell from the previous high levels to 1/10 years since the 1980s. Adult mortality in acute poisonings has increased 19% over the last 30 years. *Conclusion:* Some of the problems that lead to the establishment of FPIC have been solved, but demand for its services remains high.

#### 117. Establishing a Modern National PIC – the Estonian Experience

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*Objective:* To describe the establishment process of the Estonian Poisoning Information Centre (EPIC). *Methods:* All documents for 2000–2011 were analysed and open interviews were conducted with relevant people. *Discussion:* Initiating an EPIC had been a topic of discussion since the end of last century. The establishment process was initiated in 2000 by the Ministry of Social Affairs (MSA). A Centre for Disaster Medicine (CDM, situated in the North-Estonian Medical Centre (NEMC), had been functioning for some years and was accessible 8 h/5 days a week for doctors needing consultations on questions related to poisonings. Instead of setting up a traditional, independent centre, a PIC service with doctors on duty in ICUs was suggested. Maintaining a database with poisoning treatment monographs and collecting statistic about calls was not planned. The main attention for hospitals was focused on the allocation of additional resources from MSA. In 2003 it was decided that the PIC should be established within the MSA as a part of the Chemical Notification Centre (CNC), still with the intention to accommodate the PIC in a hospital in the future. NEMC was acting as consultant in the process and suggested hiring two emergency medical (EM) specialists for the practical establishment of the PIC. CNC cooperated with the Finnish PIC, which became a crucial partner in the further establishment of the PIC. By the end of 2004 MSA had a clear vision about the functioning of the PIC using the EAPCCT's 'Self-assessment checklist for minimum and optimum standards'. By 2005 there was a concrete plan to set up operations in collaboration with the Finnish and other Nordic PICs and to buy suitable IT software to host the database donated by FPIC. Establishment of the PIC (with funding from the State Budget) became an important priority for MSA. Two EM specialists were recruited in 2006 with a mission to initiate the centre. After a training programme in the Finnish PIC they developed the EPIC vision statement, a 5-year plan, budgets and guidelines for database security. EPIC staff started to visit EAPCCT Congresses and present the scientific work of EPIC. Discussion of the concept of the EPIC was started locally with leaders in ICU, EM, ambulance services, and hospitals to identify their expectations. In 2007 the donated monographs were translated into Estonian and updated with local information and documentation of the quality assurance process was developed. At the beginning of 2008 it was decided by PIC specialists to open the telephone lines immediately to prevent the collapse of achievements already attained. No media campaign to introduce the centre to the population and hospitals was launched, but specialists started promptly with active poisons information education (lectures, articles, interviews) for creating awareness of the PIC in the public/medical specialists. Collaboration was started with designers to create a visual corporate identity and with media specialists to draw up a full communication plan for the PIC. The PIC started operating for 8 h/5 days a week. From 2011 it became possible to open the hotline for 24 h/5 days a week. By 2010 EPIC was already well known as a source of toxicological expert advice for doctors, nurses, media, the public and State officials. EPIC has participated in updating the national emergency plan, leading an antidote program and preparing risk assessments in case of mass poisonings. *Conclusions:* From EPIC's experience in successfully establishing a sustainable PIC it is crucial to have an effective mentor-PIC, active international/domestic co-operation, clear

support and funding from the State, EAPCCT's 'minimum-optimum standards' and a couple of experienced, committed, educable EM specialists. The PIC's location within a medical institution might not have a positive effect on the establishment process, if the centre loses its independent budgeting.

#### 118. Doping and Stealing: Biscuit Poisoning

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*Objective:* To find out the agents used in biscuit poisoning and to educate travellers. *Methods:* Biscuit poisoning is defined as consumption of biscuits or drinks/beverages containing sedative agents and usually given to travellers by thieves who travel as co-passengers. Cases of biscuit poisoning admitted by railway police and recovered over the period of two years [2009 and 2010] formed the materials for the study. They were interviewed to find out the circumstances of exposure. Blood samples were analysed for toxic agents. Data were analysed statistically. *Results:* Of the 50 travellers, 15 were lone and the rest were in different family groups. The strangers were their co-passengers who talked well and started helping them or their children. After winning their confidence, they were given biscuits or drinks/beverages containing sedative agents. By 30 to 60 minutes, they started sleeping and lost their valuables. Railway police identified these sleeping passengers and shifted them to our emergency room where they were treated and recovered without complications. Toxicological analysis revealed that their blood samples contained any one of the following: midazolam, other benzodiazepine derivatives and phenobarbitone. *Conclusion:* To prevent this menace, police, railway and media authorities were alerted and travellers were educated through all audio-visual media including TV not to accept assistance, eatables and drinks from strangers or ask them buy any eatables and drinks. *Reference:* 1. Women Doping Males, Stealing Their Valuables. [http://articles.orlandosentinel.com/1987-02-09/news/0110000205\\_1\\_fort-lauderdale-detectives-rolex](http://articles.orlandosentinel.com/1987-02-09/news/0110000205_1_fort-lauderdale-detectives-rolex) [accessed 23 Nov 2011]

#### 119. Pitfalls in Communications: Medicolegal Aspects

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*Objective:* Doctors, pathologists, forensic toxicologists and generally speaking, experts' communications with patients have improved due to concerns about the medicolegal consequences of poor communication; therefore these experts should improve their communication with the mass media in order to diminish the ratio of false, accusative news about medical malpractice. *Methods:* By using the keywords "legal medicine", "crime", "autopsy", "forensic sciences", and "health", all the news data between January 2008 and December 2009 were obtained from The Media Monitoring Center in Istanbul and analyzed with the statistics program SPSS 17.0. For one of the studies, 1718 news items from 15 different

**Table 1.** Forensic news in Turkish newspapers.

Forensic Science Subdivisions	Total News (n)	Inaccurate News (n)	%	P
Autopsy	678	242	35.7	<0.001
Forensic Psychiatry	213	34	16	0.059
Forensic Pathology	163	12	7.4	<0.001
Other	148	12	8.1	<0.001
Forensic Serology	133	18	13.5	0.033
Forensic Traumatology	108	17	15.7	0.197
Forensic Anthropology	94	5	5.3	<0.001
Forensic Document Examination	82	6	7.3	0.002
Unclassified	60	7	11.6	0.091
Forensic Toxicology	39	1	2.5	0.016
TOTAL	1718	354	-	-

  

	Error		TOTAL (n)
	Absent	Present	
News about popular cases	398	30	428
News about daily cases	966	324	1290
TOTAL	1364	354	1718

Turkish newspapers were examined and 92,937 news items from all Turkish newspapers for the other study. **Results:** The legal concerns seem to form a barricade between forensic experts and mass media. Consequently, forensic experts keep a low profile in the mass media to protect their profession and to avoid any misunderstandings. As results of these studies (Table 1), we concluded that the cause of the false or accusative newsmaking against forensic experts is not malevolence but it is ignorance of the journalists about the forensic process. Accordingly, it has been observed that the mass media's attention to forensic sciences is in parallel to "popular" events and the error's percentage is low in this type of news. The error percentage was found significantly higher when the news was about clinical procedures such as autopsy. **Conclusion:** Mass media workers must receive in-job training about forensic scientific processes and forensic experts must attend media communications workshops in order to gain knowledge about the mass media's system and develop their communication skills with the journalists. **References:** 1. Chermak S. Crime in the News Media: A Refined Understanding of How Crimes Become News. In: Barak G, ed. Media, Process, and the Social Construction of Crime: Studies in Newsmaking Criminology. Garland Science, Taylor & Francis Group, 1995:95–130. 2. Sherizen, S. Social Creation of Crime News: All the News Fitted to Print. In: Winick C, ed. Deviance and Mass Media. Beverly Hills, USA: Sage Publications, 1978:203–24. 3. Lotz RE. Crime and the American Press. New York, USA: Praeger, 1991:10–11. 4. Dorfman L, Thorson E, Stevens JE. Reporting on Violence: Bringing a Public Health Perspective into the Newsroom. Health Education and Behaviour 2001; 28:402–19. 5. Guhan A, Yukseloglu E, Ersoy G, et al. Mass Media Effect on Forensic Sciences. 4th Mediterranean Academy of Forensic Sciences Meeting, Antalya, Turkey, 2009.

## 120. The Pulmonary Complications of Drug Abuse

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**Objective:** To describe the clinical effects of various recreational drugs on the lungs. **Discussion:** The use of

the lungs as a route of entry for recreational substances is based on their large surface area and excellent blood supply. These factors allow soluble substances rapid entry into the blood, with correspondingly high peak blood concentrations. Both acute and chronic use of abused substances can damage pulmonary tissue and is associated with diverse complications through diverse mechanisms. However, parenteral administration of these same substances may also be associated with adverse pulmonary effects. Pulmonary complications may include indirect effects, such as infections (e.g. Staphylococcus aureus, tuberculosis, HIV/AIDS), aspiration pneumonia, or septic embolism from endocarditis. Barotrauma, such as pneumothorax, may result from an intensive valsalva maneuver due to breath-holding in an attempt to absorb maximal drug. Parenteral drug use may result in microparticle-induced interstitial fibrosis or pulmonary infarction (e.g. talc, silica). Cocaine, particularly in the smokeable, alkaloidal form (i.e. crack), is the illicit drug whose abuse is highly associated with pulmonary consequences, sometimes called "crack lung." Smoking of cocaine exposes the lung directly to the volatilized drug producing profound vasoconstriction that leads to nonspecific histopathological changes. Crack cocaine, due to the need for high temperatures for volatilization, produces thermal airway injury, and is associated with basal cell hyperplasia and ciliary dysfunction. Aspiration of crack pipes is also relatively frequent. Inhaled and parenteral use of heroin and other opioids are associated with acute lung injury (ALI) following respiratory depression in overdose. The primary manifestation of ALI is alveolar edema, and may be due to several disparate mechanisms, with or without an association with naloxone administration. Mechanisms include valsalva maneuver against a closed glottis (Muller maneuver) pneumocyte hypoxia, and myocardial stunning due to catecholamine excess. Many of the effects of inhaled drugs are due to a non-specific inflammatory mechanism, through activation of neutrophils and production of inflammatory mediators of oxidative stress. Bronchospasm is a common manifestation of airway inflammation. Tobacco based drugs, such as marijuana, carry many of the same irritating effects as cigarettes, and heavy use results in chronic cough and sputum production. Other substances inhaled for recreational purposes, including amyl and butyl nitrites, methamphetamine, and phencyclidine, may be associated with bronchospasm, pulmonary inflammation, and barotrauma. The lungs, which act as both a barrier to

the external environment and a conduit into the systemic circulation, may themselves be damaged by drug use in recreational users. **Conclusion:** The lungs are highly susceptible to both acute and long term consequences of the use of recreational drugs. Mechanisms of toxicity include direct irritation during inhalation, physiological alterations following other routes of administration, or mechanical compromise due to barotrauma. **References:** 1. Reid PT, Macleod J, Robertson JR. Cannabis and the lung. J R Coll Physicians Edinb 2010; 40:328–3. 2. Restrepo CS, Carrillo JA, Martínez S, et al. Pulmonary complications from cocaine and cocaine-based substances: imaging manifestations. Radiographics 2007; 27:941–56. 3. Tashkin DP. Airway effects of marijuana, cocaine, and other inhaled illicit agents. Curr Opin Pulm Med 2001; 7:43–61. 4. Wolff AJ, O'Donnell AE. Pulmonary effects of illicit drug use. Clin Chest Med 2004; 25:203–16.

## 121. Respiratory Consequences of Chemical Warfare Agents

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**Objective:** To review the respiratory consequences of chemical warfare agents. **Discussion:** Chemical warfare agents (CWA) are weapons that work principally through toxicity, causing death, permanent harm or temporary incapacitation. They are classified into six groups: 1. Nerve agents: sarin, soman, tabun and VX. 2. Vesicants: sulfur mustard (SM) and lewisite. 3. Choking or respiratory agents: chlorine and phosgene. 4. Blood agents: cyanide. 5. Psychotropic agents: quinuclidinyl-benzilate. 6. Non-lethal agents including riot controllers e.g. tear gases. Chlorine and SM were largely used during World War I. SM, tabun and sarin were widely applied during the Iraq-Iran war in 1983–88.<sup>1</sup> They have induced a lot of morbidity and mortality, mostly due to pulmonary consequences. However, their mechanisms of toxicity are different and thus the respiratory complications are varied. Nerve agents: the nerve agents (NA) are extremely potent organophosphorus compound cholinesterase inhibitors, and are the most toxic of the known chemical weapons.<sup>2</sup> The main effects of NA include cholinergic (muscarinic and nicotinic) syndromes and CNS toxicity. However, respiratory tract is the most affected organ, either as a result of the neurotoxic effects inducing pulmonary oedema, respiratory depression and even respiratory muscle paralysis due to the intermediate syndrome. The Iraqi army used tabun in Majnoon Island (1984) and sarin in Halabjah (1988) which induced a lot of morbidity and mortality due to respiratory failure.<sup>2,3</sup> Sarin was also used in terrorist attacks in Matsumoto (1994) and in the Tokyo metro (1995) with high respiratory involvement as rhinotracheobronchitis, respiratory depression, pulmonary oedema leading to death in a few patients.<sup>3</sup> Antimuscarinic (atropine) and anticholinergic (oximes) are well known antidotes for OP compounds and have been used for more than six decades, but their therapeutic effects are controversial.<sup>4</sup> Sulfur mustard: SM is an alkylating agent that initially reacts with ocular, respiratory and cutaneous tissues resulting in acute poisoning and even death. Acute toxic effects of SM appear after variable periods of latency (minutes to weeks) depending on the dose, mode of exposure, environmental temperature, and on the individual. The most targeted organ is the lungs with several pathologies, ranging from acute bronchitis to bronchopneumonia, ARDS and even pulmonary emboli, which

induce mortality particularly in the second week after SM exposure.<sup>5</sup> Delayed toxic effects of SM in Iranian veterans 16–20 years after SM exposure were found in the lungs, peripheral nervous system, immune system, skin and eyes,<sup>6</sup> which are different from the early toxic effects<sup>7</sup>. The late respiratory complications were chronic bronchitis, chronic obstructive pulmonary disease, bronchiectasis, asthma, large airway narrowing, and pulmonary fibrosis.<sup>6,7</sup> Immunosuppression has been a main problem for the moderate to severely SM poisoned patients since their exposure which has caused recurrent infections and even mortality.<sup>6–8</sup> We have observed delayed complications on the upper respiratory tract, even with malignancies.<sup>8,9</sup> Lewisite: This arsenical vesicant (2-chlorovinylchloroarsine) was developed during World War I, but was not used. Lewisite toxicity is similar to that of SM, resulting in dermal and mucous membrane damage with conjunctivitis, airway injury, and vesiculation, but less secondary infection. Its specific known antidote is British anti-Lewisite.<sup>1</sup> Pulmonary agents: Although both pulmonary agents (chlorine and phosgene) were not used in large scale after World War I (WWI), the risk of exposure remains because of their extensive use in industry, or possibly as a terrorist weapon. When released on the battlefield, chlorine forms a yellow-green cloud with a distinct pungent odour detectable at levels that are not immediately dangerous. Phosgene is either colourless or seen as a white cloud as a result of atmospheric hydrolysis. Both chlorine and phosgene produce injury by hydrolysis to hydrochloric acid in the lungs. Battlefield exposure induces cough, chest discomfort, dyspnoea, lacrimation, and asphyxiation. Acute tracheobronchitis, bronchopneumonia and pulmonary oedema may develop causing respiratory failure and death. Prolonged observation after phosgene exposure is the rule, as some casualties had initially appeared well and had been discharged, but unfortunately returned in severe respiratory distress a few hours later during WWI. The average estimated recovery time was 60 days for chlorine and 45.5 days for phosgene. There is no known effective antidote for chlorine, but N-acetyl cysteine was described as an antidote for phosgene.<sup>1</sup> Respiratory consequences of the other CWA agents are not prominent to be described here. *Conclusion:* Respiratory system is the target organ for most CWA particularly chlorine, phosgene, SM and Lewisite. Delayed respiratory complications of SM have been major health problems for the veterans of WWI and the Iraq-Iran war. *References:* 1. World Health Organization. Public health response to biological and chemical weapons: WHO guidance - 2nd ed. Geneva, 2004. Available at <http://whqlibdoc.who.int/publications/2004/9241546158.pdf> [accessed 12 Dec 2011]. 2. Balali-Mood M, Balali-Mood K. Nerve Agents. In: Brent J, Wallace K, Burkhart K, eds. *Critical Care Toxicology*. 1st ed. Philadelphia, USA: Elsevier Mosby, 2005:1379–93. 3. Balali-Mood M, Balali-Mood K. Neurotoxic disorders of organophosphorus compounds and their managements. *Arch Iran Med* 2008; 11:65–89. 4. Balali-Mood M, Shariat M. Treatment of organophosphate poisoning. Experience of nerve agents and acute pesticide poisoning on the effects of oximes. *J Physiol Paris* 1998; 92:375–8. 5. Balali-Mood M, Hefazi M. The pharmacology, toxicology, and medical treatment of sulphur mustard poisoning. *Fundam Clin Pharmacol* 2005; 19:297–315. 6. Balali-Mood M, Hefazi M, Mahmoudi M, et al. Long-term complications of sulphur mustard poisoning in severely intoxicated Iranian veterans. *Fundam Clin Pharmacol* 2005; 19:713–21. 7. Balali-Mood M, Hefazi M. Comparison of early and late toxic effects of sulfur mustard in Iranian veterans. *Basic Clin Pharmacol Toxicol* 2006; 99:273–82. 8. Balali-Mood M,

Afshari R, Zojaji R, et al. Delayed toxic effects of sulfur mustard on respiratory tract of Iranian veterans. *Hum Exp Toxicol* 2011; 30:1141–9. 9. Zojaji R, Balali-Mood M, Mirzadeh M, et al. Delayed head and neck complications of sulfur mustard poisoning in Iranian veterans. *J Laryngol Otol* 2009; 123:1150–4.

## 122. Non-Occupational and Occupational Lead Exposures Reported to the UK National Poisons Information Service 2008–2010

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*Objective:* To ascertain the number of enquiries to the UK National Poisons Information Service (NPIS) regarding non-occupational and occupational exposure to lead. *Methods:* The study involved the retrospective analysis of data collected between 1st January 2008 and 31st December 2010. *Results:* The NPIS received 418 telephone enquiries regarding 359 patients exposed to lead over this period. In 274 of these 359 patients (76.3%) the exposure was non-occupational and the most common source of lead was from paint-stripping (n = 58). The two main routes of non-occupational exposure were ingestion (n = 121) and inhalation (n = 109). Seventy-four of the 274 patients exposed non-occupationally were children ≤ 4 years of age, the majority of whom (n = 54) were exposed by ingestion; 15 were exposed by inhalation. The mean (± SD) blood lead concentrations in the children exposed by ingestion and inhalation respectively were 44.3 ± 20.4 µg/dL (n = 12) and 15.78 ± 6.39 µg/dL (n = 5) [p < 0.01]. Eighty-five exposures were occupational with inhalation (n = 79) being the commonest route of exposure; painters and decorators were the most common occupational group involved (n = 22). The age group with the highest number of occupationally exposed patients was 30–39 years (n = 26); this group accounted for 31% of the total occupational exposures. Lead concentrations are available in 74 of the 274 patients (27.0%) exposed non-occupationally and in 54 of the 85 patients (63.5%) exposed occupationally. The highest blood lead concentrations were 198 µg/dL (non-occupational group) and 149 µg/dL (occupational group). The mean (± SD) blood lead concentrations in the non-occupational and occupational groups respectively were 36.1 ± 34.4 µg/dL (n = 74) and 51.5 ± 29.9 µg/dL (n = 54) [p < 0.01]. Twenty-six of the 54 patients occupationally exposed had blood-lead concentrations ≥ 50 µg/dL, which represents a minority of the 672 workers with blood lead concentrations ≥ 50 µg/dL reported to the UK Health and Safety Executive over the same period. Chelation therapy was recommended or had been given previously in 21 patients; 14 of these were exposed non-occupationally. *Conclusion:* Despite the toxicity of lead being well known, lead exposure remains a cause of morbidity not only in industry but also to members of the public, particularly to children.

## 123. New Biomarkers for Drug-Induced Hepatotoxicity

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*Background:* Serum biomarkers of drug-induced hepatic injury and functional recovery guide treatment

decisions. Serum biomarkers, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), and alkaline phosphatase are the most common markers of injury used in clinical practice and drug development. Unfortunately, these injury enzymes do not predict tolerance or adaptation to a drug exposure with functional recovery. Serum transaminases may increase manifold after exposure only to return to baseline despite continued drug exposure. Therefore, better biomarkers that predict serious life threatening hepatotoxicity are needed. In clinical practice prothrombin time and serum bilirubin are followed to monitor hepatic functional recovery. *Discussion:* Several additional hepatic enzymatic biomarkers are undergoing investigation.<sup>1</sup> Sorbitol dehydrogenase and glutamate dehydrogenase are mitochondrial enzymes released secondary to injury. Glutathione-S-transferase is a phase II detoxification enzyme concentrated in the centrilobular region that may be more sensitive than ALT. Malate dehydrogenase is a Krebs' Cycle enzyme predominant in the periportal region. Purine nucleoside phosphorylase is an enzyme in the purine salvage pathway found in high concentrations in hepatic endothelial cells. Paraoxonase-1 (PON-1) represents a down regulation marker, not a leakage enzyme, as levels fall during hepatic injury. PON-1 is a HDL-associated esterase that protects LDL from oxidative modifications. MicroRNA (miRNA), specifically miR-122, appears to be an earlier marker than ALT of hepatotoxicity. MiR-122, however, has a short half-life and may not be predictive of outcome.<sup>2</sup> Toxicogenomic analyses including Genome Wide Association Studies (GWAS) and Candidate Gene Association Studies (CGAS) have uncovered predictive genetic biomarkers.<sup>3</sup> Genetic variants of CYP2C, uridine diphosphate glucuronyltransferase 2B7 (UGT2B7), and glutathione-S-transferases (GSTs) are associated with increased risk for hepatotoxicity from NSAID, isoniazid, and troglitazone exposure.<sup>3,4</sup> HLA variants such as HLA-B\*5701 are associated with an increased risk for hepatotoxicity from flucloxacillin.<sup>4</sup> Transcriptomic evaluation of hepatotoxicity may generate a set of genomic biomarkers useful to preclinical drug development. Microarray analyses of *in vitro* human hepatocytes compare hepatotoxic drugs to create gene expression signatures. Toxicity related genes recognized by one group included genes associated with calcium ion binding and catalytic activity, peptidase activity and drug response genes including CYPs and drug transporters, cytokine binding and the inflammatory response, as well as DNA repair and cytotoxic T cell differentiation.<sup>5</sup> Metabonomics is the comprehensive and quantitative analysis of endogenous and exogenous metabolites. The metabolic profile before, during and after exposure to acetaminophen and ximelagatran has been studied and may yield predictive toxicity insights.<sup>6</sup> Proteomics also holds the promise to identify new serum biomarkers.<sup>7</sup> New mass spectrometric techniques have been applied to proteomics that can identify low concentrations of peptides and proteins that have undergone post translational modifications. Two examples of modified proteins that have been evaluated in hepatotoxicity are keratin-18 (K18) and high-mobility group box-1 protein (HMGB1).<sup>8</sup> Full-length K18 is an indicator of necrosis, while the caspase cleaved K18 indicates apoptosis. Hypoacetylated HMGB1 also indicates necrosis, while the hyperacetylated form is released from activated innate immune cells indicating an inflammatory response to the hepatotoxicity. Currently these molecular forms of K18 and HMGB1 provide mechanistic insights into hepatocyte death. The measurement of K18 and HMGB1 serum levels was more sensitive than ALT

levels in detecting acetaminophen hepatotoxicity. The potential utility of measuring the serum molecular forms of K18 and HMGB1 levels and needs further clinical evaluation in drug-induced hepatotoxicity and hepatic recovery. The complexity of hepatic injury and recovery suggests that a combination of these biomarkers will provide the best sensitivity and specificity for hepatic injury and recovery. **Conclusion:** New biomarkers for drug-induced hepatotoxicity are undergoing development and clinical evaluation. It is likely that new panels of liver biomarkers will emerge from ongoing toxicogenomic, toxicometabolic, and toxicoproteomic research. **References:** 1. Ozer J, Ratner M, Shaw M, et al. The current state of serum biomarkers of hepatotoxicity. *Toxicology* 2008; 245:194–205. 2. Starkey Lewis PJ, Dear J, Platt V, et al. Circulating microRNAs as potential markers of human drug-induced liver injury. *Hepatology* 2011; 54:1767–76. 3. Agundez JAG, Lucena MI, Martinez C, et al. Assessment of nonsteroidal anti-inflammatory drug-induced hepatotoxicity. *Expert Opin Drug Metab Toxicol* 2011; 7:817–28. 4. Daly, AK. Drug-induced liver injury: past, present and future. *Pharmacogenomics* 2010; 11:607–11. 5. Cheng F, Theodorescu D, Schulman IG, et al. *In vitro* transcriptomic prediction of hepatotoxicity for early drug discovery. *J Theor Biol* 2011; 290:27–36. 6. Robertson DG, Watkins PB, Reilly MD. Metabolomics in toxicology: pre-clinical and clinical applications. *Toxicol Sci* 2011; 120(S1):S146–70. 7. Amacher DE. The discovery and development of proteomic safety biomarkers for the detection of drug-induced liver toxicity. *Toxicol Appl Pharmacol* 2010; 245:134–42. 8. Antoine DJ, Williams DP, Kipar A, et al. High-mobility group box-1 protein and keratin-18, circulating proteins informative of acetaminophen-induced necrosis and apoptosis *in vivo*. *Toxicol Sci* 2009; 112:521–31.

#### 124. Cases of Human Exposure Identified in 2006–2010 by the Italian Surveillance System of Toxic Exposures and Poisonings

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<sup>1</sup>National Institute of Health (ISS), Rome; <sup>2</sup>Poison Control Centre of Milan, Niguarda Cà Granda Hospital, Milan; <sup>3</sup>Poison Control Centre of Naples, Cardarelli Hospital, Naples; <sup>4</sup>La Sapienza University, Rome, Italy

**Objective:** The Italian National Institute of Health, in collaboration with the Poison Control Centres (PCCs) in Milan and Naples, implemented in 2006 a national system for surveillance of toxic exposures and poisonings (STEP). The aim of the present contribution is to provide a preliminary characterization of human exposures transmitted to STEP by the collaborating PCCs in 2006–2010. **Methods:** Descriptive analyses of the case data collected and notified to STEP according to standard procedures. **Results:** During the first five years of activity, STEP detected 230,818 cases of human exposure. Altogether, about 43% of the cases were aged less than 6 years. Male and female individuals were equally distributed. About 89% of exposures occurred at home, 3% in the workplace, and 2% were due to environmental pollution. Reason for exposure was unintentional for about 77% of cases, mainly related to uncontrolled access to the agent (40%), therapeutic error (7%), pouring from the original container to another (5%). Intentional circumstances were reported for 19% of the cases

and were mainly due to suicide attempt (16%). Clinical effects possibly related to exposure were coded in 39% of cases, while at least one treatment was required for 66%. About 40% of the cases were exposed to pharmaceuticals and 58% to non pharmaceuticals. The most common categories of agents were: cleaning substances (household) (19%), sedative/hypnotic/antipsychotic (11%), pesticides (7%), analgesics (6%), foreign bodies, antidepressants, cosmetics/personal care products (5%, respectively). **Conclusion:** PCCs are an important source of routinely collected data on human toxic exposures and poisonings.<sup>1</sup> These data can be used for improving public health at local, national, regional and global level.<sup>2</sup> In Europe, guidelines should be developed to facilitate common data collection by PCCs, their use and comparison. **References:** 1. Watson AW, Litovitz TL, Bedson MG, et al. The Toxic Exposure Surveillance System (TESS): risk assessment and real-time toxicovigilance across United States poison centers. *Toxicol Appl Pharmacol* 2005; 207:S604–10. 2. WHO, ILO, UNEP. International Programme on Chemical Safety. Report. Workshop on poisons centres and the use of human data in consumer product risk assessment. Berlin, 9 May 2005. Available on: [http://www.who.int/ipcs/publications/methods/workshop\\_report.pdf](http://www.who.int/ipcs/publications/methods/workshop_report.pdf) [accessed 16 Dec 2011].

#### 125. Heavy Metal Exposures Reported to the UK National Poisons Information Service 2008–2010

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**Objective:** To investigate the epidemiology of exposures to “heavy metals” in the United Kingdom. **Methods:** In the three year period from 2008 to 2010, the UK National Poisons Information Service collected prospectively 1198 telephone enquiries relating to 14 heavy metals (aluminium, antimony, arsenic, bismuth, cadmium, chromium, copper, cobalt, lead, mercury, manganese, selenium, thallium and zinc), accounting for 0.7% of all enquiries. **Results:** There has been a gradual decline in the number of enquiries relating to heavy metals from 456 in 2008 to 335 in 2010. The majority of exposures were accidental (84%) occurred more commonly in males (55.2%) than females (40.5%). Most exposures occurred at home (64.1%), 16.7% at work and 11.0% at school. Seventy per cent were acutely exposed with chronic exposures accounting for around 12% of enquiries. Exposures in children nine years of age or less accounted for 25.4% of the enquiries, with 20% of all enquiries concerning children 5 years of age or less. Mercury was the most commonly implicated agent (n = 508; 42.4%), followed by copper (n = 179; 14.9%), lead (n = 144; 12.0%), zinc (n = 109; 9.1%) and aluminium (n = 107; 8.9%) with the remaining metals accounting for 13% of reported cases. In 1141 of the 1198 enquiries, the Poisons Severity Score (PSS) was recorded at the time of the enquiry. The majority of patients were asymptomatic (63.5%), 32.5% had developed minor features, 3.5% moderate features and only 0.5% severe features (PSS3). Those with severe features were exposed to zinc (n = 2) from multivitamins and herbal products, copper oxide by inhalation of anti-fouling paint (n = 1) and arsenic (n = 3). Of the 508 enquiries relating to mercury, 261 (51.4%) related to thermometers (room, fish tank or body) and 92 (18.1%) occurred in children five years of age or less. 93.5% of all cases were asymptomatic or had minor features only and none developed severe features. **Conclusion:**

Exposures to heavy metals are relatively infrequent and have been declining in the UK. Incidents relating to mercury thermometers are the most common cause of heavy metal exposure.

#### 126. Unique Product Identifier for Improvement of Risk Assessment in European Poison Centres

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**Objective:** Fast, reliable and precise identification of a product (‘mixture’ in EU legislation) and its specific formulation is a prerequisite for correct medical risk assessment after a potentially toxic exposure. Identification based on the product’s trade name can be time consuming: callers often experience difficulties in finding the complete trade name, and notifications of product information to Poison Centres do not always include all names mentioned on the product label. We propose the implementation of a Unique Product Identifier (UPI) on the label of products marketed in the EU and its inclusion in all notifications of mixture formulations to Poison Centres in particular according to CLP Regulation article 45. **Methods:** Discussion within the EAPCCT Working Group on Poison Centres Activities. **Results:** The proposed UPI format (“AA-XXXX-XXXX-YYYY-KK”) starts with 2 letters representing the official Member State code (“AA”). It is followed by the company unique VAT Identification Number (VATIN) that is converted by an algorithm into 2 blocks of 4 characters (“XXXX-XXXX”). Next is the formulation code (FC) of 4 digits (“YYYY”), able to distinguish over 106 formulations for each notifying company. The UPI ends with a checksum-control-key (“KK”) (calculated from AA + the encoded VATIN + FC). This standardised UPI format can be autonomously generated with a public algorithm by companies, without the need for a centralized administration. The German Federal Institute for Risk Assessment (BfR) has developed a standard (EN 15178)<sup>2</sup> describing a graphical symbol, to be placed near the barcode together with the UPI for easy recognition of this element. **Conclusion:** The proposed UPI provides a unique link between product (label) and notified product formulation and it can easily be generated by companies themselves. In addition, the UPI might also be useful to identify mixtures that are used as ingredients in mixtures. The UPI will serve as a link to separately notified mixtures when the supplier does not make the mixture formulation available to the notifier, protecting industrial and commercial confidentiality. **References:** 1. <http://upi.toxalert.fr> [accessed 22/11/2011]. 2. Hahn A, Rickert D. CEN Standard (EN 15178:2007) for improvement of product identification at poison centers. *Clin Tox* 2008; 48:627.

#### 127. Poisons Training for Paramedics

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**Objective:** Ambulance paramedics, often the first point of contact with poisoned patients, need to make rapid assessments and instigate appropriate emergency treatment plans. To do so effectively they require speedy access to relevant information. This outreach programme was established to ensure that all ambulance personnel in Wales and South West England are familiar with the full range of resources offered by The National Poisons Information Service (NPIS). **Methods:** All ambulance stations in Wales and the South West (173) were contacted by letter and/or telephone and provided with the following information: 1. General information about NPIS and a request that all ambulance crews be made aware of the NPIS 24/7 poisons enquiry telephone number. 2. Information relating to TOXBASE®, the primary toxicology database of the NPIS, and an encouragement to each station to apply for free registration. (Telephone number and website information were also provided in the form of stickers and postcards for ease of dissemination and availability to individual crews) 3. NPIS (Cardiff) offers free hands-on training for ambulance personnel in the efficient use of TOXBASE®. Consultant clinical toxicologists are also available to provide training in the basic management of poisoned patients including recognition of toxidromes and signs and symptoms relating to the severity of poisoning; training courses often being structured to the specific requirements of individual cohorts. **Results:** Since the outreach programme began, TOXBASE® registrations from ambulance stations have increased 31% in Wales and 44% in the South West. There has also been a very positive response to the offer of specialist training; overall 217 ambulance personnel have received training from poisons information specialists and clinical toxicologists on the efficient use of TOXBASE® and other aspects of poisoning in 13 separate training sessions. Six specialist training sessions have also been held for 42 members of the South West England Hazardous Area Response Team (HART). **Conclusion:** Specialised training greatly enhances the confidence of paramedics when dealing with poisoned patients. In cases where there remains uncertainty regarding the potential toxicity of agents, access to TOXBASE® or the poisons enquiry line provides invaluable reassurance and markedly reduces the costs associated with unnecessary transport and accident and emergency admission.

### 128. Role of the Poison Control Center of Morocco in the Improvement of Poisoning Management

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**Objective:** The purpose of this study was to demonstrate the role of the Poison Control Center of Morocco (CAPM) in improving poisoning management and in anticipating toxic risk in comparison with international standards.<sup>1,2</sup> **Methods:** A retrospective study of poisoning cases reported to the poison center between 1980 and 2008 was conducted. An analytical study focused on controlling the epidemiological profile of toxic exposures, use of gastric emptying and symptomatic treatment, availability of antidotes, standardization of poisoning management and its impact on the outcome of poisoning. The triggering of alerts was also studied. **Results:** Between 1980 and 2008, the CAPM has received about 260,000 declarations; among which 66% were represented by scorpion stings and envenomation, other causes in 32% and requests for laboratory analyses

in 2%. The use of gastric emptying decreased from 45% to 4% of cases. A national strategy was set up for stings and scorpion envenomation enabling improvement in lethality from 1.54% to 0.22%. Several alerts were triggered and enabled anticipation of the risk by removing or rationalizing the use of certain products. A review of the center was established for information, education, and public and media awareness. Training of health professionals has been possible through the establishment of a degree in toxicology. **Conclusion:** The skills developed in humans and the material resources allocated to the poison center in Morocco and its actions have improved the indicators of morbidity and mortality of poisoning and achieved the goal of having a clear vision for the next decade. **References:** 1. Sanfaçon G. Role d'un centre antipoison en santé publique. In: Gérin M, Gosselin P, Cordier S, et al., eds. Environnement et santé publique - Fondements et pratiques. Edisem / Tec & Doc, Acton Vale / Paris, 2003:863-70. 2. Lignes directrices pour la lutte contre les intoxications. Programme International sur la Sécurité Chimique (IPCS). Genève; 1998.

### 129. Important Milestone in the Harmonisation of Product Notification

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**Objective:** By 20 January 2012 the European Commission (EC) had reviewed the possibility of harmonising product information notified by companies to poisons centres or governmental authorities, according to article 45(4) CLP Regulation. Poisons centres' needs should play a leading role in the harmonization process. **Methods:** The EAPCCT Working Group on Poisons Centres Activities / European Regulatory Issues developed new EAPCCT Product Information Guidelines in 2010. In 2011, these guidelines were discussed with industry associations, governmental authority representatives of EU Member States (MS) and EC to find consensus on notification format and procedures. **Results:** Some industry associations questioned the need for additional information beyond Safety Data Sheets. The EAPCCT reconfirmed that additional information, a complete ingredient list and exact concentration for substances with high hazard classifications are required for adequate clinical risk assessment (i.e. the task for which they are responsible). The EC supports the EAPCCT approach as a reasonable compromise between the various current national requirements in MS. However, the EAPCCT was requested to accept small concentration ranges for high hazard ingredients and concentration thresholds for notification of non-classified ingredients (the EAPCCT Working Group will investigate these requests). Furthermore, the EAPCCT proposed a Unique Product Identifier on every product label for non-ambiguous product formula identification and as a link to the corresponding product information notified. This was resisted by industry but supported by the EC. A cost/benefit analysis is to be performed. For easy product data exchange a harmonised electronic XML-based format will be developed. Moreover, most stakeholders favour setting up a European product database. The EC will explore the feasibility. **Conclusion:** As there was agreement between all stakeholders, EC is expected to recommend harmonisation of product notification. The

EC will present the harmonisation review at a meeting of Competent Authorities on REACH and CLP (CARA-CAL). If harmonisation is further supported by MS, a legislative proposal will be developed that will add a procedure for harmonized product data notification as an Annex to the CLP Regulation. In this case, European harmonisation of product notification by industry to poisons centres is a substantial step closer to realisation.

### 130. Role of the Poison Control Center of Morocco in the Identification and Prevention of Poisoning: The Example of Ricinus communis Poisoning

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**Objective:** To demonstrate the role of the Poison Control Center in the identification and prevention of poisoning, especially in children. We illustrate with cases of accidental poisoning by the seeds of the castor oil plant in children. **Case series:** During the month of September 2011, the Poison Control Center was contacted several times about emergencies in the region of Kenitra with a probable case of poisoning in children for which the toxic substance was unknown. Six children, between 7-11 years, all presented with neurological disorders especially clouding of consciousness. One of the six patients had convulsions. The children vomited some seeds between 2 and 6 hours after exposure, had abdominal cramps, and some had diarrhea. Before the symptoms, the doctor of the poison control center considered poisonous plants and asked that photographs of the seeds found in the vomit be sent by email. Once the picture of the seed was received, the plant was identified (*Ricinus communis*), and the course of action was dictated. The Poison Control Center considered it necessary to notify public health authorities in the region so that care could be taken to prevent such poisonings being repeated. **Conclusion:** Poison Control Center staff have training and experience in recognizing problems of toxicity and so play a crucial role in the prevention of poisoning.

### 131. Electronic Cigarettes: Risk Assessment

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**Objective:** Electronic cigarettes (EC) are nicotine delivery devices. The regulatory status of EC in France and the European Union is unclear and distribution of these devices is not controlled. The French Health Products Safety Agency asked the National Coordination Committee for Toxicovigilance to assess the risks related to the use of EC. This assessment focused on the risk of acute nicotine poisoning (due to accidental exposure of children and under normal conditions of use) and the risks related to repeated exposure. **Methods:** Nicotine contents of EC were obtained from packaging information or commercial web sites, and by measurements on samples distributed in France. A retrospective analysis of EC exposure cases in French Poison and Toxicovigilance centres was also performed. **Results:**

EC compositions are generally not in accordance with French regulations. In most cases, incomplete or unusable information was available on the packaging, and on websites selling these devices. The amounts of nicotine measured in 20 cartridge samples from the French market were generally higher than those announced on the packaging (sometimes, twofold or even higher). These measurements indicated that the nicotine content of cartridges labelled 16 mg was sometimes as high as 34 mg. The nicotine content of vials labelled 6 mg was as high as 112 mg (7 mL; 16 mg/mL). These nicotine contents exceed the waiver limits of European Regulation 1272/2008 on hazardous substances in consumer products applied to electronic cigarettes. To estimate the risks related to acute nicotine toxicity, a minimum lethal dose by ingestion in adults (40–60 mg) and a toxic dose in children (1.4 mg/kg) were used. To reach toxic doses, adults and children would need to ingest 1.4 or 0.4 refill cartridges (containing 34 mg of nicotine), or 3 mL or less than 1 mL of liquid from a refill bottle (concentration 16 mg/mL), respectively. **Conclusions:** A retrospective review of cases collected by the French poison and toxicovigilance centres from 1999 to 2010 revealed 8 cases of exposure to electronic cigarettes: 6 were symptomatic and none were severe (irritation 4, headache 2, palpitations 2, dizziness 1).

### 132. Immediate Packaging of Healthcare Products: Confusions between Plastic Single Dose Packaging Notified to French Poison and Toxicovigilance Centres

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**Objective:** Confusion between plastic single dose packaging is very frequent. The French Health Products Safety Agency asked the National Coordination Committee for Toxicovigilance to evaluate and characterize the cases notified to the French Poison and Toxicovigilance Centres (FPTCs). The aim was to make an as complete as possible assessment of confusion between single dose packaging, in order to target the risk reduction measures. **Methods:** Prospective multicentre study spanning two months – one in spring, the other in autumn – including all the cases where a patient was exposed by mistake to a single dose packaged solution, whatever the route of administration and the packaged products (drugs, biocide, cosmetics, etc.). **Results:** 169 cases in the two months (68 and 101 respectively) were analysed. They showed that parents (79%) and patients themselves (16%) were the origin of the confusion, which happened most frequently at home (96%). Cases were symptomatic in 38% of exposures and two serious cases were observed. Infants less than 5 years old represented the most affected age group (79%). Furthermore, the most serious complications largely involved infants (apnea, aspiration pneumonia). Seventy-nine per cent of the cases resulted from intranasal instillation and 14% from ocular administration. Antiseptic solutions (sodium borate, chlorhexidine solution, hydrogen peroxide, antiseptics dyes, etc.) were the main products (88%) involved in these acci-

dents. In most of these cases (80%) they were administered instead of saline solution. This fact explained the age of the patients. The root cause analysis showed that there were multifactorial causes related to human factors (135 cases) and/or to the product itself (151). **Conclusion:** These accidents were not rare (probably more than 1000/year in the FPTCs) and often due to the product itself. Risk minimisation measures are necessary to decrease the risk of confusion: improving the appearance of single dose packaging, especially their labelling, would lead to a better identification of the products. If the immediate packaging of single doses of saline solution was made more easily recognizable, either visually (e.g. thanks to coloured doses) or to the touch (e.g. with marking as for blind people), then the risk of confusion would most likely be reduced, at least quantitatively.

### 133. Poison Information Centre's Call Responder – An Additional Competency for Emergency Medicine Nurses?

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**Objective:** To describe the Estonian Poisoning Information Centre's (EPIC) choice of call responders on behalf of emergency medicine (EM) nurses. EPIC's mission is to provide adequate advice quickly so as to reduce the incidence of illness, damage to health and death as a result of severe cases of poisoning. PICs often have to deal with poisoning cases where the source and substance of the toxin is unknown. In different poisons centres call responders may be pharmacists, nurses, junior physicians, and clinical toxicologists. Currently all call responders in EPIC are emergency medicine nurses (EMN). **Methods:** Analysis of the compatibility of study programmes for EMN and pharmacists in Estonian health care colleges with guidelines for EPIC call responding described in the Poisoning Management Process Flow chart. **Results:** The nurse specialist in intensive care and EM is competent to provide independent nursing care at all levels of healthcare including intensive care nursing and team leading in ambulance brigade services. The study programme for a nurse specialist includes 3.5 years basic nursing education, 2 years of practice as a general nurse, plus a specialization course lasting a year. Emergency nurses are experienced in triage and the practice of providing first aid guidelines, thus having an advantage in interviewing cases where the source of poisoning is not known or the fact of poisoning is not sure. The objective of the 3 year training programme for pharmacists is to train specialists competent in the field of pharmaceutical products and the pharmaceutical production process. Pharmacists have an advantage when the source of poisoning is known. **Conclusion:** In circumstances when a clinical toxicologist is not easily available PIC call responders council poisoning victims, interpret clinical conditions and identify the possible toxic agent. Best prepared for this are EMNs, whose course of study requires work experience in emergency situations and is directed to making independent treatment decisions in any health endangering circumstance. Pharmacological emergencies are just one branch of all the toxicological emergencies the PIC has to cope with, while toxicological emergencies are just one branch of all acute situations nurse-specialists of emergency medicine are trained to cope with. Establishing an additional toxicology nurse specialisation within the emergency nursing specialisation course might be of value.

### 134. Child Medication Errors in Morocco

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**Objective:** To describe the medication errors occurring in children less than 15 years old. **Methods:** Prospective study of all medication errors collected in the Poison and Pharmacovigilance Center of Morocco in 2008. The parameters analyzed were: age, sex, route of administration, the type and level, persons who could be responsible for the error, symptoms and outcome. **Results:** 62 cases of medication errors were collected. The average age of our patients was 3.71 ± 2.98 years; the sex-ratio was 2.8 in favor of males. The newborn age group was concerned in 26 cases followed by toddlers in 20 cases and 16 cases in children. The oral route was found in 41 cases followed by the rectal route in 17 cases. One third of our patients (20 cases) were symptomatic with predominantly nausea. There was an error of dose in 34 cases, of product in 17 cases. Nineteen cases of dose errors are made by a family member, 7 cases by the prescribing doctors and 2 cases by the nurse. The action to be taken was based on medical surveillance and symptomatic treatment. An antidote was administered in 5 cases. The outcome was favorable in 100%. **Conclusion:** All players in the processing circuit (family, doctor and nurse) are involved at their respective levels. Significant efforts must be intensified by all the links in the chain of the circuit including the family to prevent and mitigate the consequences.

### 135. Huge Differences in the Risk Perception between Pregnant or Lactating Women and Poisons Information Specialists

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**Objective:** Each year the Norwegian Poisons Information receives about 600 calls where the risk of the foetus or breastfed infant has to be considered. These enquiries are challenging, primarily due to vague literature and anxious callers. Very few studies have examined how the counselling professionals themselves perceive such risks. However, studies have shown that pregnant and lactating women often have an unrealistic fear of exposure. There are numerous sources of this misinformation. It is likely that an excessive risk perception of counselling professionals will be reflected in the women. The aim of this ongoing study is to compare the risk perception of pregnant and lactating women to that of the staff at the Poisons Information Centre (PIC). We also evaluated the scientific evidence for the PIC's advice and how the women rate the value of the advice. **Methods:** The women's own risk perceptions as to whether the exposure could endanger the foetus or infant (scale 0–10) were collected before counselling. After literature search and counselling, the poisons information specialists (SPIs) scored their own risk perception (scale 0–100%). Further information was collected during a structured telephone interview. **Results:** In the period May–October 2011, 68 enquiries have been enrolled in the study. In total, 21 out of 68 women perceived that the risk was ≥ 5 (scale 0–10). In 18 of these 21 enquiries the SPIs considered the exposure to involve no risk at all. In only two out of 68 enquiries did the staff judge the risk to be above 1%. During the counselling pro-

cesses, the SPIs used more than 20 different toxicological sources, primarily teratological books and databases. The women considered the encounter with the PIC as trustworthy and rated the value of the answer to 8.4 on average (scale 0–10). **Conclusion:** Huge differences in risk perception exist between the pregnant or lactating women and SPIs. As in this study, risk communication should be a two way process in which professionals and patients exchange opinions and information. In the event of establishing a Teratology Information Service, the PIC would be a most relevant academic base for such an activity.

### 136. Remote Botanical Identification in the Management of Plant Poisoning: A Useful Telemedicine Experience

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**Objective:** Plant identification is crucial for adequate management in several cases of plant poisoning. The identification of plants can be confirmed by a botanist through the evaluation of a good quality picture jointly with some information on the characteristics of the plants. The utility and efficacy of this procedure was evaluated in all cases of plant poisoning managed by the Pavia Poison Centre (PPC) when associated with transmission of picture(s), in order to (i) optimize the botanist evaluation, (ii) identify factors that can prevent plant identification, (iii) define the useful information about the plants and the characteristics that the image must have to allow recognition. **Methods:** All cases of plant poisoning referred to PPC during 5-years (2007–2011) in which at least one image (picture obtained by mobile or camera) was sent to us for plant identification were retrospectively analysed. Data on the plants, the picture, and the clinical manifestations were considered. Reasons that prevented the recognition of certain plants were evaluated. **Results:** In the considered period, PPC registered 1050 cases of plant poisonings. In 105 cases (10%) the plant was unknown, and in 45 of these (43%) an image was sent to PPC. The image allowed plant identification in 28 cases (62%); in 9 the identification of a non-toxic plant allowed the immediate discharge of the patient. In 17 cases (38%) the identification of the plants was not possible because of lack of useful image details for recognition (8 cases), poor image quality (7 cases) and insufficient information on the plant's characteristics (2 cases). Based on these critical issues, a procedure to optimize the effectiveness of remote recognition has been developed establishing the information useful for plant identification (some characteristics of plants and leaves) and how best to capture the image (i.e. the parts of the plant to be photographed, type of background, how to cut berries and bulbs). **Conclusion:** The study demonstrates the usefulness of telemedicine tools and remote expert botanical identification in the management of plant poisonings, and allowed the improvement of procedures to optimize the transmission of pictures with a consequent improvement in the clinical management.

### 137. The Safety of Duloxetine in Overdose: A Poison Center Review

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**Objective:** Duloxetine is a serotonin and norepinephrine reuptake inhibitor which is mainly used to treat major depressive disorders. The safety profile of single agent duloxetine ingestions has never been systematically reviewed. The objective for this study is to describe the demographic and clinical outcomes of single agent duloxetine ingestions reported to the National Poison Center Data System (NPDS) of the American Association of Poison Control Centers (AAPCC). **Methods:** NPDS data was searched for all duloxetine exposures between 2004 and 2010. **Results:** 29,438 cases of duloxetine exposures were reported between 2004 and 2010. Multidrug ingestions, non-human ingestions, non-oral exposures and adverse drug reactions were excluded and 11,447 ingestions were analyzed. 4764 (42%) cases occurred in patients less than 6 years old. In 3173 (28%) cases, the ingestion was intentional and in 8105 (71%) ingestion was unintentional. 8.79% (1006) cases were judged to be potentially toxic but unable to be followed. One death (0.01%) was reported and 0.27% (31) were judged to have a major outcome. 4.4% (508) were classified as moderate outcomes. 84.5% (9672) of cases were classified as no effect, minimal effect and not followed but judged to have nontoxic exposure. 2% (229) cases had unrelated effects with the exposure thought to not likely be responsible for the effect. Clinical events were documented in 71% of cases. The most common overall clinical events were drowsiness/lethargy (7.5%), vomiting (4.6%), tachycardia (4.1%), nausea (3.7%), dizziness/vertigo

**Table 1.** Carisoprodol exposures and subsets.

No.	Age	Subset	Cases in 2010	Ratio (2011/2000)	Ratio (2009/2004)	Rsquare (N = 12)
1	All	All Exposures	8625	1.22	1.07	0.921
2	All	Caller Site = HCF	6579	1.57	1.20	0.982
3	All	Caller Site = Hospital ED	6295	1.53	1.18	0.975
4	All	Caller Site = Free-standing ED	124	2.95	1.84	0.813
5	All	Reason = Abuse (intentional)	1136	1.71	1.17	0.891
6	All	Reason = Misuse (intentional)	789	1.41	1.17	0.825
7	10–19 y/o	All Exposures	1022	0.67	0.78	0.943
8	>50 y/o	All Exposures	1519	2.43*	1.52	0.993
9	>50 y/o	Reason = Suicide (suspected)	798	2.99*	1.62	0.985
10	>50 y/o	Reason = Misuse (intentional)	150	2.96*	1.83	0.944
11	>50 y/o	Reason = Abuse (intentional)	141	3.79*	1.87	0.968
12	>50 y/o	Reason = Unknown (intentional)	84	5.74	1.96	0.960
13	>50 y/o	Reason = Unknown	55	6.55	1.81	0.815

\*Quadratic (2nd order) regression term statistically significant and positive (> 0).

(2.2%), agitation/irritability (2.3%). Other serious notable clinical events included seizure (0.2%), coma (0.3%), dysrhythmias (0.1%), fever/hyperthermia (0.2%), respiratory compromise (0.1%), and conduction disturbances (0.2%). **Conclusion:** The majority of duloxetine single agent ingestions were generally safe but in patients that became ill, there were clinical events that are linked to greater morbidity/mortality. This can be secondary to dose ingested or patient comorbidities. Strengths of our study include the ability to collect data reported to all US poison centers and the large sample size of our study population. Limitations include potential miscoding of data and missing information. There is also reporting bias including the potential of underreporting of nontoxic exposures. Future studies are needed to verify our findings.

### 138. National Poison Center Data System Carisoprodol Encounters 2000 – 2011

Spyker DA<sup>1</sup>, Bronstein AC<sup>2</sup>.

<sup>1</sup>Uniform Services, University of the Health Sciences, Bethesda, MD; <sup>2</sup>Rocky Mountain Drug & Poison Center, University of Colorado School of Medicine, Denver, CO, US

**Objective:** The Substance Abuse and Mental Health Services Administration (SAMHSA) reported that carisoprodol abuse and misuse tripled in individuals > 50 years old from 2004–2009. We examined changes over time (COT) in carisoprodol exposures in the National Poison Data System (NPDS) focusing on patients > 50 years-old. **Methods:** We analyzed closed Drug ID and Exposure calls to AAPCC centers from 1-Jan-2000 through 8-Nov-2011. We examined COT by 2nd order (quadratic) regression of subsets by age, Caller Site and Reason for Exposure as a percent of Exposure calls (to normalize the incomplete 2011 data and reduce dependence on secular changes in total Exposure calls). We calculated the ratio of exposures from the regression equation for 2009/2004 and 2011/2000. **Results:** Carisoprodol was one of the substances in 94,567 of the 28,208,270 Exposures. Of these, 57.2% were multi-substance (64% from health care facilities), and 26.5% involved a benzodiazepine and 8.67% ethanol. Table 1 shows the results for carisoprodol Exposures, and 12 subsets of Exposure calls. Increase ratios (2011/2000) ranged from 1.22 to 1.66. Regressions 9–12 had a statistically

significant ( $p < 0.05$ ) positive quadratic term (COT was increasing at an increasing rate). **Conclusion:** NPDS data support the emergence of the use and abuse of carisoprodol in individuals > 50 y/o, and with most recent data, show several categories are increasing at an increasing rate.

### 139. Consumer Exposure Calls to US Poison Centers

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<sup>1</sup>Rocky Mountain Drug & Poison Center, Denver Health, Denver, CO; <sup>2</sup>Uniformed Services University of the Health Sciences, Bethesda, MD, US

**Objective:** A major value of poison centers is the ability to manage poisoning exposures without the need

**Table 1.** Mean number of calls/year and the percentage change over time of calls by Reasons.

Reason	All Calls				Health care facility				Own Residence			
	Num Calls	/yr	/yr <sup>2</sup>	COT	Num Calls	/yr	/yr <sup>2</sup>	COT	Num Calls	/yr	/yr <sup>2</sup>	COT
Adverse reaction - Food	5,070	+	-	∩	296	-		∩	4,252	+	-	∩
Intentional - Misuse	46,974	+	+	/	13,129	+	+	/	25,028	+	+	/
Intentional - Suspected suicide	195,474	+	+	/	138,691	+		/	35,330	-	-	\
Other - Contamination/tampering	5,624	+		/	465			/	4,293	+		/
Other - Withdrawal	939	+	-	/	417	+		/	459	+	-	∩
Unintentional - General	1,433,548	-		\	105,061	-		\	1,211,144	-		\
Unintentional - Therapeutic error	228,021	+	-	/	15,717	+	-	/	189,119	+		/

+ / - indicates coefficient for /yr or /yr<sup>2</sup> was positive(+) or negative (-) and statistically significant (p < 0.05), ∩ / \ indicates the general shape and position of the quadratic regression of the COT

for emergency medical services. We hypothesized that the fraction of consumer calls managed at home would be stable despite a change in the total number of calls. **Methods:** We examined number of calls, percent of total (%) and change over time (COT) for National Poison Data System (NPDS) exposure calls from Consumers calling from Own Residence (CCOR), Health Care Facilities (HCF) and all calls (All) for Reason and Management Site. **Results:** NPDS logged 28.25 million (m) calls from 1-Jan-2000 to 12-Nov-2011. CCOR median [range] was 1.80 [1.46, 1.85] m/yr; % managed at home was 88.4% [88.2, 89.0]. Table 1 shows the mean number of calls/year and the COT % of calls by Reasons. All 7 reasons had a statistically significant linear slope (/yr) for All and CCOR, and 5 of the 7 for HCF calls. There was general agreement (increase or decrease) across All, HCF and CCOR. The greatest rate of increase was seen for Unintentional-Therapeutic Error (All and CCOR), and Intentional-Suspected Suicide (HCF). **Conclusion:** A high proportion of cases are managed at home without the need for emergency health care provider referral. The % of CCOR managed at home was constant at 88.4% despite COT in the Reasons and number of exposures.

were obtained using a standardized data template with written definitions. Rates are reported as number of exposures reported per 100,000 population. **Results:** Seven countries participated; Australia, Germany (Göttingen), Italy, Netherlands, Switzerland, United Kingdom (UK) and US. All centres manage calls from health care providers. Australia, Italy, Germany, Switzerland and US manage calls from the public as well. All countries reported increased oxycodone rates during the study period ranging from 30% to 410% (Table 1). Five of 7 countries reported increased buprenorphine rates (range 11–295%) while Germany and Italy reported decreases of 14% and 49%, respectively). Four of 7 countries reported increased methadone rates (range 4–29%) while Netherlands, UK and Australia reported decreased methadone rates (range 5–11%). **Conclusions:** Oxycodone exposures reported to poison centres in all participating countries increased during the study period. Methadone rates were relatively unchanged during the study period, yet larger increases were reported in some countries for buprenorphine. While these data illustrate rates over

time within each country, one cannot compare rates between countries due to variation of data collection methods (some centres accept calls from the public, some do not). Additional data on reporting bias, drug availability, drug supply source, and types of exposures reported are required to further understand these findings.

#### 141. “Por Çöz” - A Europe-Wide Prohibition Process

Hahn A, Begemann K, Feistkorn E, Meyer H. *Federal Institute for Risk Assessment (BfR), Berlin, Germany*

**Objective:** A two-years eleven-month-old girl ingested a Turkish rust remover and descaling agent “Por Çöz” containing nitric acid. This cleaning product was sold especially in Turkish retail stores in Germany. Immediately the little girl suffered from severe manifestations: reduced consciousness, vomiting, caustic burns in the oesophagus and stomach, aspiration pneumonia. After

#### 140. International Perspective of Prescription Opioid Exposures Reported to Poison Centres from 2007–2010

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<sup>1</sup>Rocky Mountain Poison & Drug Center, Denver Health, Denver, CO, US; <sup>2</sup>National Poisons Information Service (Newcastle Unit), Newcastle upon Tyne; <sup>3</sup>National Poisons Information Service (Cardiff), Cardiff, UK; <sup>4</sup>Swiss Toxicological Information Centre, Associated Institute of the University of Zurich, Switzerland; <sup>5</sup>GIZ-Nord Poisons Centre, University Medical Center Göttingen, Germany; <sup>6</sup>NSW Poisons Information Centre, The Children’s Hospital Westmead, Sydney, Australia; <sup>7</sup>Milan Poison Center, Azienda Ospedaliera Ospedale Niguarda Ca’ Granda, Milan, Italy; <sup>8</sup>National Poisons Information Centre, Utrecht, The Netherlands

**Objective:** Prescription opioid abuse has been deemed as epidemic in the United States (US). Abuse in other countries is not well studied. The objective of this study is to characterize human exposures to specific prescription opioids reported to poison centres from multiple countries over a 4 year study period. **Methods:** Human exposures to oxycodone, buprenorphine, and methadone reported to poison centres from 2007–2010

**Table 1.** Prescription opioid exposure rates as reported by poison centres by country 2007–2010.

Country in % Change Rank Order	Exposure rate per 100,000 population				Rate change (first rate reported to 2010)	% change (first rate reported to 2010)
	2007	2008	2009	2010		
<b>OXYCODONE</b>						
Italy	0.008	0.007	0.038	0.043	+0.034	+410%
Switzerland	0.159	0.369	0.302	0.525	+0.366	+230%
Netherlands	0.190	0.238	0.212	0.392	+0.203	+107%
Australia	1.904	2.142	3.010	3.286	+1.382	+73%
Germany	0.212	0.348	0.280	0.364	+0.152	+71%
United States	3.497	4.193	4.535	4.856	+1.359	+39%
United Kingdom	NR	0.099	0.145	0.128	+0.029	+30%
<b>BUPRENORPHINE</b>						
Netherlands	0.012	0.037	0.024	0.048	+0.036	+295%
United States	0.413	0.684	0.835	0.944	+0.530	+128%
Australia	0.337	0.419	0.499	0.530	+0.192	+57%
Switzerland	0.238	0.198	0.342	0.289	+0.050	+21%
United Kingdom	NR	0.104	0.121	0.115	+0.012	+11%
Germany	0.167	0.144	0.182	0.144	-0.023	-14%
Italy	0.045	0.052	0.033	0.023	-0.022	-49%
<b>METHADONE</b>						
Italy	0.096	0.107	0.096	0.123	+0.028	+29%
Germany	0.432	0.402	0.455	0.500	+0.068	+16%
Switzerland	1.112	1.147	1.131	1.220	+0.108	+10%
United States	1.186	1.172	1.232	1.230	+0.044	+4%
Netherlands	0.514	0.488	0.461	0.489	-0.025	-5%
United Kingdom	NR	0.206	0.171	0.188	-0.018	-9%
Australia	0.607	0.586	0.583	0.539	-0.068	-11%

NR = not reported.

12 days on the intensive care unit the clinical course was stabilized, so that she was transferred to the children's medical unit. Six weeks after starting inpatient treatment the little patient could be discharged to ambulant treatment with an application of a gastric fistula. About ten months after the poisoning accident repeated follow-ups showed a pleasant healing process. **Results:** Investigation of BfR case-enquiries together with the German Poison Centers with detailed identification of the products involved resulted in 134 case reports concerning the rust remover and descaling agent "Por Çöz". The survey between 1999 and 2010 showed that the product contains about 25% nitric acid and caused severe damage to health (caustic burns as well as inhalation trauma). Based on the data of the BfR-Hazard Survey, the BfR-Rapid Communication targeted the Turkish manufacturer, the German distributor and the responsible ministries; the resulting summary BfR-Risk Assessment Report gave the German Federal Environmental Agency (UBA) the opportunity to inform the EU-Commission and the other Member States about the temporary prohibition on the German market. The health risk of the cleaning product "Por Çöz" containing nitric acid could be proved to the EU with the article 45 Detergents Regulation at the 29th of October, 2010. **Conclusion:** The EU-Commission has approved the prohibition of the placing of the product "Por Çöz" on the German market for another year and verifies the possibility of a permanent restriction for using nitric acid in the field of consumers. In addition the BfR submitted a request to the European Chemicals Agency (ECHA) for a well-defined Europe-wide new chemical risk assessment of nitric acid via a CLH-Report – Proposal for Harmonised Classification and Labelling. All these measures will probably ensure that the dangerous chemical nitric acid will be withdrawn from the European consumer market.

#### 142. EU Regulation for Uncoloured Paraffin Lamp Oils and Grill Lighters for Consumers

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<sup>1</sup>Federal Institute for Risk Assessment (BfR); <sup>2</sup>Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU), Berlin, Germany

**Objective:** Owing to the ban on coloured and scented lamp oils labelled with R65 and the introduction of substitutes in 2000 in European countries, the health risk due to lamp oil accidents in children had been reduced. But an increasing risk involved in clear and uncoloured paraffinic hydrocarbons labelled with R65 resulting from rising sales of lamp oils and grill lighter fluids of this type has offset the risk minimization effect established in Germany from 2000 onwards. **Methods:** Since uncoloured lamp oils with the same composition and grill lighter fluids were not affected by the ban, poisonings continued to occur. Despite repeated warnings, serious accidents involving lamp oils and grill lighter fluids happened time and again, since children continued to drink them inadvertently. Two children died in 2004 in Germany. An analysis of all poisonings revealed that grill lighter fluids which have the same composition in terms of substances as paraffin-containing lamp oils increasingly caused serious poisonings in children between 2002 and 2008. For this reason Germany forcefully advocated a further tightening of the regulations on a European level and demanded the inclusion of grill lighter fluids. **Results:** The European Commission submitted a proposal for a regulation which was approved by member states and entered into force on 1 December 2010. From then on, lamp

oils and grill lighter fluids with a paraffin base may only be sold in black, opaque containers not exceeding one litre. The containers must now be marked indelibly with the additional phrase "Just a sip of lamp oil – or even sucking the wick of lamps – may lead to life-threatening lung damage" or "Just a sip of grill lighter may lead to life-threatening lung damage". In addition, decorative oil lamps for the general public shall not be placed on the market unless they conform to the European Standard on Decorative oil lamps (EN 14059) adopted by the European Committee for Standardisation (CEN). **Conclusion:** No later than 1 June 2014, the Commission shall request the European Chemicals Agency to prepare a dossier with a view to banning grill lighter fluids and fuel for decorative lamps, labelled R65 or H304.

#### 143. Improvements to the UK's Online Poisons Information Database, TOXBASE® – Reducing Unsuccessful User Searches

Jackson G, Lupton DJ, Bateman DN.

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**Objective:** To examine new functionality provided to TOXBASE® by Speed-Trap Analytics. A key feature of this facility is to allow the National Poisons Information Service (NPIS) to identify unsuccessful user searches. During its pilot phase Speed-Trap data was analysed to demonstrate proof of concept for this facility. **Methods:** During the month of October 2011 a selection of unsuccessful user searches were identified and considered for inclusion on TOXBASE®. **Results:** Unsuccessful user searches mainly occurred because users misspell existing TOXBASE® entries. Amitriptyline and quetiapine are existing TOXBASE® entries that were commonly mis-spelled by our users. Table 1 provides examples of unsuccessful user searches that occurred because there was no specific entry on TOXBASE®. Unsuccessful user searches identified by Speed-Trap Analytics that lead to additions to TOXBASE® included 4-AcO-DMT (4-acetoxy-N,N-dimethyltryptamine), a research chemical and Viegax, a venlafaxine containing product available in Israel.<sup>1</sup> **Conclusions:** NPIS now has a unique insight into TOXBASE® usage through dynamic collection technology. Identification of unsuccessful user searches ensures that NPIS is in a position to keep TOXBASE® up to date with the latest information, particularly for emerging drugs of abuse. In addition, when common mis-spellings of existing TOXBASE® entries are identified they can be added as a synonym or a "sound alike" link to the existing entry. NPIS are now in a position to reduce the number of unsuccessful TOXBASE® user searches. **Reference:** 1. Sweetman

S. Martindale: The Complete Drug Reference. 37th ed. London, UK: Pharmaceutical Press, 2011: Vol B:3520.2.

#### 144. Improvements to the UK's Online Poisons Information Database, TOXBASE® – Real Time Alerting

Jackson G, Lupton DJ, Bateman DN.

National Poisons Information Service (Edinburgh Unit), Royal Infirmary, Edinburgh, UK

**Objective:** In order to enhance its utility TOXBASE® is now supported by Speed-Trap Analytics providing the National Poisons Information Service (NPIS) with a real time alerting system. This facility allows NPIS to immediately follow-up TOXBASE® accesses to entries identified as being of particular interest. Within 5 minutes of an access being made an email alert is automatically generated detailing the page accessed, and by whom. We report a demonstration of proof of concept during pilot studies of the system in October 2011. **Methods:** During the month of October 2011 all automatic email alerts were analysed. The alerting tag was added to 13 chemical agents of interest (3-quinuclidinyl benzilate, adamantane, ammonia, carbon monoxide, chlorine, dioxins, formaldehyde, hydrofluoric acid, phosphoric acid, sarin, sodium selenite, sulphur mustard and sulphur trioxide). **Results:** During October 2011 there were 575 emails received detailing 604 alerts. The majority of the alerts (435) originated in England, alerts were also received from other EU countries (Belgium and Poland) as well as Australia and Brazil. Alerts most commonly detailed accesses to carbon monoxide (306), chlorine (105) and hydrofluoric acid (56). The majority of alerts were received from hospital A&E departments (264) and from non-educational NHS Direct/24 users (123). There were 43 clusters of alerts (defined as 5 or more alerts to the same agent on the same day) that may have warranted follow up e.g. on the 3rd Oct carbon monoxide was accessed by 2 different UK poison centres, 7 A&E departments in 7 different towns and 1 NHS 24 department, as detailed in 15 alerts. **Conclusion:** NPIS now has a unique insight into TOXBASE® usage through dynamic collection technology. As NPIS offers a 24-hour service it can act promptly on real time alerts. NPIS can also now consider accesses made to pages of interest in different hospitals across different regions as a whole in real time. The alerting facility will soon be enhanced to include information on whether or not TOXBASE® accesses relate to specific patients and, therefore, guide NPIS as to which accesses should be followed up urgently.

**Table 1.** Examples of unsuccessful user searches on TOXBASE® in October 2011.

Search term entered	By	When	Term is
4-AcO-DMT	A&E dept. (UK)	08/10/2011	4-Acetoxy-N,N-Dimethyltryptamine – a research chemical
DMT	Poisons Centre (UK)	11/10/2011	Dimethyltryptamine
Muchozol	Poisons Centre (Poland)	18/10/2011	A Polish insecticide product
Qualitek	Poisons Centre (Iceland)	17/10/2011	A soldering product
Skintruth	Paediatric A&E dept. (UK)	12/10/2011	A skin care range
Viegax	NHS Direct* (UK)	09/10/2011	A venlafaxine containing product available in Israel <sup>1</sup>

\* Public access health information service.

#### 145. Usage and User Experience of an Online Clinical Toxicology E-Learning Resource

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**Objective:** TOXlearning, the UK clinical toxicology e-learning resource developed by NPIS Edinburgh, went live in September 2005 providing training on using TOXBASE®; additional modules were added in July 2008 (Management of the poisoned patient) and September 2010 (Management of patients involved in chemical incidents). The objective of this work was to identify users' usage patterns, and assess their experience of the resource. **Methods:** Web usage statistics were analysed. All users since 2005 were e-mailed a quality assurance questionnaire and returns analysed. **Results:** At 30/09/11 3270 individuals had registered since the site's launch; 2905 completing modules on the first unit, 690 the second, 161 the third. Users have training-level access to TOXBASE®, the UK clinical toxicology database. The top TOXBASE® monographs accessed closely matched the main substances covered in the first module (e.g. anti-freeze/ethylene glycol, paracetamol, ferrous sulphate, etc). As newer modules came online covering different topics, hits on corresponding monographs rose up the ranks (e.g. from the second module digoxin rose from 77th to 18th; from the third module sulphur mustard and carbon monoxide ranked for the first time). Only 2425 users' e-mail addresses remained valid; 59.4% (1439) "official" addresses/40.6% (986) private accounts. Responders were ambulance staff 28.1% (37), nurses 21.2% (28), doctors 18.1% (24), NHS 24/Direct 16.6% (22), and other 15.9% (21). All user types responded similarly and positively when asked to grade statements concerning ease of access, attractiveness of resource and ease of navigation. On a scale of 1–6 (1 = disagree completely/6 = agree completely) they agreed "a lot" or "completely" that learning was pitched at the right level (75.0% [99]), and that the subject matter was interesting (88.6% [117]). On a scale of 1–5 (1 = very poor/5 = very good) 93.3% (124) rated their overall satisfaction 4 or 5. **Conclusion:** As potentially 7 years could have passed since first registration the response rate (5.6% [135]) was, as expected, low. A large proportion of users registered using private e-mail accounts to facilitate learning from home. Users took the opportunity to use training-level access to TOXBASE® to support their e-learning activities. Irrespective of user type respondents indicated a high degree of confidence and satisfaction with the resource.

#### 146. Social Networking and Novel Drugs of Abuse: How Information Regarding "Bath Salts" is Disseminated on Facebook

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**Objective:** Since 2004, there has been an explosion in the use of social networking sites (SNS). To date, there are no studies examining how information on novel drugs of abuse is disseminated or accessed through these sites. We sought to describe how information about "bath salts" was portrayed on Facebook. **Methods:** We generated a list of search terms related to "bath salts". Over a period of two days (August 2011) we performed a search of Facebook groups and pages for each of the predefined search terms. The results were reviewed and unrelated groups and pages were discarded. For each result we recorded the title, date found, number of followers, date of most recent post, and

geographic location. We then characterized each result with respect to the following: accounts of personal use; encouraged or discouraged use; gave medical information about bath salts; gave information about how to use or purchase bath salts; whether the stated objective of the page or group supported banning or legalizing bath salts. **Results:** Our search results generated 82 pages and 145 groups. The total number of "likes" or "followers" was 72,092. The majority (50%) had 11–100 "followers" or "likes" with only 5% having greater than 1000 "followers" or "likes". The majority (53%) presented information aimed at discouraging the use of bath salts. However it is noteworthy that 29% encouraged its use, 31% gave information about where to purchase such drugs, and 23% gave medical information about bath salts. **Conclusion:** SNS such as Facebook establish a medium by which users can easily publish information, opinions and advertisements regarding "bath salts". While the majority of discourse was aimed at discouraging the use of bath salts, a significant proportion of sites encouraged its use and attempted to provide medical information and purchasing information. SNS may provide a means by which poison control centers can discover trends in the use of novel drugs, public perceptions and perceived medical knowledge about such drugs, and provide a point of intervention to reach out to the public.

#### 147. Methylene Chloride Poisoning with Delayed Carboxyhemoglobinemia Treated with Hyperbaric Oxygen Therapy

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**Objective:** Methylene chloride, or dichloromethane (DCM), is a halogenated hydrocarbon used as an industrial solvent and is a common constituent of commercially available paint strippers. *In vivo* the parent compound is metabolized by CYP2E1 to carbon monoxide and may result in consequential carboxyhemoglobinemia. Reports of successful treatment with hyperbaric oxygen therapy (HBOT) are limited and no clinical guidelines for the management of exposed patients exist. We report DCM intoxication with resulting carboxyhemoglobinemia successfully treated with sequential HBOT. **Case report:** A 45 year-old previously healthy man experienced loss of consciousness while using a DCM-containing solvent to strip paint from an old bathtub. Co-workers discovered the patient unconscious lying in a pool of solvent approximately 3 hours from the time he was last seen. Prehospital vitals included pulse, 54/min; BP 154/80 mmHg; respirations 24 shallow and labored. On arrival the patient was lethargic with the following vital signs: pulse 74 beats/min; BP 147/98 mmHg; respirations 20 breaths/min; temperature 98 F; and O<sub>2</sub> saturation of 98%. Non contrast CT of the brain, ECG, and laboratory values were within normal limits. The patient's mental status cleared over 2 hours of observation and discharge was anticipated. Prior to discharge a carboxyhemoglobin level was found to be 5.4%. Transfer to a HBO facility was initiated and on arrival he received standard 46 minute hyperbaric oxygen treatment with 100% oxygen at 2.8 atm. He complained of persistent dizziness and a COHb level several hours later was 17.3%. Four subsequent HBO treatments were provided over the course of 2 days; the patient's symptoms completely resolved and COHb levels trended to 2.2%. He was discharged in his baseline state of good health and experienced no neurological sequelae on follow-up. **Discussion:** DCM toxicity results in a biphasic toxicity pattern. Depression of mental status and respiratory drive from anesthetic

effect of halogenated hydrocarbons are seen immediately post-exposure. Subsequently, CO poisoning may occur from metabolism of the parent compound. HBO therapy is efficacious in treating CO toxicity but does not prevent metabolism of DCM to CO by CYP 2E1. Future treatment options may include preventing DCM metabolism and warrant investigation. **Conclusion:** DCM poisoning warrants inpatient observation, serial CO levels, and treatment of CO toxicity with HBOT as appropriate.

#### 148. Epidemiology of Work-Related Chemical Exposures Presenting to an Emergency Department in Singapore, a 4 Year Review: 2007 – 2010

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**Objective:** Singapore is a small industrialized island state where 25% of the 5 million people are non-resident population. Chemical injuries can occur during work and a study of these exposures would help improve worksite safety. **Methods:** Work related chemical exposure cases were identified from Emergency Department (ED) computerised records. Injuries due mainly to heat, electricity, trauma and mechanical injuries were excluded. The case records were traced and abstracted by trained assistants. **Results:** 240 cases were identified with an average of about 60 cases per year. Most of the patients were male (92%) and young adults (73% between 20–40 years old). Forty-nine per cent of the workers were foreign workers. Most of them were technicians, cleaners and labourers (53%) and worked mainly in the construction and manufacturing industries (47%). All the exposures were acute and the majority of the workers presented within 4 hours of incident (51%) with chemical exposure to their eyes (52%) and skin (31%). There were some cases of inhalation (27 cases) and ingestion of chemicals (10 cases). The majority of the chemicals involved were corrosives (41%), hydrocarbons (17%), and cleaning solutions (9%). However, the chemical names were identified in only 35% of cases and the safety data sheet was only available in 2% of cases. Eighty-four per cent of the workers did not have any personal protective equipment documented. Pre-hospital decontamination (eye and skin irrigation) was performed for 53% of the workers. Similar decontamination was performed for 48% of the workers in the ED. Antidote treatment with calcium gluconate for hydrofluoric acid exposure was used for 5 patients. There were 6 incidents with 2 or more casualties involved and 3 of these incidents involved inhalational exposure. Only 11% of patients were admitted and most of the patients recovered uneventfully. Four patients had surgical procedures and 5 patients had complications. **Conclusion:** Work related chemical exposure that presents to the ED are mainly exposures to the skin and eye. Most of the workers do well with immediate decontamination and first aid but antidotes are required for some exposures.

#### 149. Respiratory Disorders after Exposure to High-Level Ozone from a Deodorizer

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**Objective:** Report of an accidental exposure to dangerous levels of ozone including clinical data, lung function and simulation of exposure. **Methods:** Retrospective case series. Index case examined for persistent dyspnoea 3 months after acute exposure to ozone and identification of additionally seven cases with similar exposure. All were examined clinically and with lung function test. Discharge records were evaluated for persons treated at hospital. Exposure was assessed by a simulated scenario and by individual history. **Results:** Exposure was caused by an UV-driven ozone generator installed in the cooker hood of a professional kitchen in order to abate the foul smell in the environment. By mistake switches for ventilation and ozone generator were dissociated, thus ozone could be generated without being ventilated through the exhaust pipe. For one week following the installation ozone was smelled in the kitchen and minor symptoms were reported. The night between days seven and eight ventilation had been stopped, while the generator worked. The morning crew were met by a pungent smell and had respiratory symptoms within seconds following entering the kitchen. Subsequently they worked for a few hours with open windows before the source of the smell was identified. Simulation demonstrated ozone levels at 0.7 ppm and 20 ppm following 5 and 60 minutes respectively with ventilation off and generator on. Seven of eight exposed persons had respiratory and/or general symptoms. One person had hemoptysis, one had reduced oxygen saturation acutely and reduced ventilatory capacity and hyposmia for several months. No others had abnormal lung function and none had abnormal lung x-ray. **Conclusion:** To our knowledge, this is the first description of exposure from a powerful ozone generator wrongly installed with mismatching ventilation. The most severely exposed individuals may have been in an atmosphere of 20 ppm ozone or even higher for more than half an hour. This can be compared to the IDLH value of 5 ppm. Fifty ppm for 30 minutes is considered potentially fatal. **Reference:** 1. Baxter P, Aw TC, Cockcroft A, et al., eds. *Hunter's Diseases of Occupation*. 10th ed. London, England: Hodder Arnold 2010.

#### 150. Withdrawn

#### 151. A Case of Acute, Local Neurotoxicity Following Cutaneous Exposure to a Phenoxyethanol Solution Used as an Anesthetic in Fry

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**Objective:** To describe a case of local neurotoxicity following cutaneous exposure to phenoxyethanol. **Case report:** In order to distinguish between individuals, fry of Atlantic salmon were tagged with a non-fluorescent dye. The dye was injected into the yolk sack of anesthetized fry using a 1 mL syringe and needle. Fish were anesthetized in a 500 mg/L phenoxyethanol solution in Petri dishes. On the first day of tagging the procedure

was performed without gloves and consequently the operator was exposed to phenoxyethanol repetitively over a period of approximately 2 hours. Day 2 the operator felt numbness and loss of sensitivity in the right thumb and index-finger, both used for the procedure. He also felt the strength of his biceps was diminished. The numbness vanished completely within three months whereas, the reduced strength of contraction of right arm disappeared within a month. The salmon showed no signs of adverse reactions to the anesthetic. **Discussion:** Phenoxyethanol belongs to the group of glycol ethers; it is commonly used as an anesthetic in fish hatcheries. Phenoxyethanol is known to have a high permeability through skin. In a previous report<sup>1</sup> dealing with three women working in a salmon hatchery using phenoxyethanol as an anesthetic, for tagging and fin-trimming salmon, fish were picked up bare-handed from dishpans containing water with phenoxyethanol added as an anesthetic (unknown concentration). When using phenoxyethanol they noticed headache and symptoms of intoxication. After a couple of hours this was followed by diminished strength and sensation of hands and fingers, particularly of the hand used to pick up the fish. After 1 to 2 years of exposure, the workers experienced onset of cognitive impairment. Phenoxyethanol has been shown to cause a dose related significant reduction in membrane currents induced by treatment with receptor agonists in *in vitro* experiments in rat-brain glutamate receptors. Disturbances of the receptors may lead to decreased neuronal activity, an effect resembling that of other organic solvents. These effects are consistent with the symptoms of neurotoxicity reported for the three women occupationally exposed to phenoxyethanol. **Conclusion:** In our case the symptoms occurred acutely and only local symptoms were described. The toxicological mechanisms proposed explain the observed symptoms. Appropriate gloves are recommended for the described procedure. **Reference:** 1. Morton WE. Occupational phenoxyethanol neurotoxicity: a report of three cases. *J Occup Med* 1990; 32:42-5.

#### 152. Lead Exposure's Effect on Hearing Frequencies in Battery Workers

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**Objective:** One of the adverse health effects of elevated exposure to lead among adults is damage to the auditory system. Studies have reported that adults with long term lead exposure can exhibit ototoxicity. The main objective of this study was to evaluate the effect of blood lead level on human audiological frequencies in battery workers in Iran. **Methods:** This study was conducted in an acid-battery manufacturing factory and 428 workers with mean age 39.8 years were recruited from all over the factory. Personal information such as demographics and work history was obtained through a questionnaire. All subjects took part in an audiometric examination of hearing thresholds, for both ears, with air-conducted pure tones at frequencies of 500, 1000, 2000, 4000, 6000 and 8000 Hz and audiological frequencies were used as biomarkers for ototoxicity in adults with chronic lead exposure. Subjects' blood samples were collected and analyzed for levels of lead with inductive couple plasma-mass spectrometry. All statistical analyses were performed with SPSS 11.5. In exploratory data analysis, mean ( $\pm$  standard deviation) for quantitative variables, frequency (per cent) for qualitative variables and Spear-

man & Mann Whitney correlation coefficients were computed to explore the significance of relationships among covariates. Statistical significance was defined as P value < 0.05. **Results:** Average blood lead concentration was 39.80 micrograms/dL, mean hearing threshold for both ears in different frequencies was obtained, and their average noise exposure level was 86.0 dBALeq. Multivariate analysis, in which possible risk factors of hearing ability were considered, demonstrated that there was no significant correlation between a high, long-term lead exposure and hearing frequencies. **Conclusion:** Among the subjects of the present study, the workers did not show significant differences between hearing frequencies in groups with different blood lead levels. The results persisted after adjustment was made for age. **References:** 1. Counter SA, Buchanan LH. Neuro-ototoxicity in andean adults with chronic lead and noise exposure. *J Occup Environ Med* 2002; 44:30-8. 2. Park SK, Elmarsafawy S, Mukherjee B, et al. Cumulative lead exposure and age-related hearing loss: the VA Normative Aging Study. *Hear Res* 2010; 269:48-55.

#### 153. Lead Acetate May Cause Erectile Dysfunction by Modulating the Action of Nitric Oxide in Rat Corpus Cavernosum

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**Objective:** Despite the fact that metal toxicity has been widely reported in industrial toxicological studies, very little has been reported about the effect of acute and chronic lead exposure on erectile function in men and animals. **Methods:** Rats were injected with lead acetate (0.25 - 0.5 - 2 mg/kg) intraperitoneally. After 21 days, intracavernosal pressure/mean arterial pressure (ICP/MAP) in response to nerve stimulation, nitric oxide production, malonaldehyde, glutathione levels and superoxide dismutase activity in corpus cavernosum, kidney and brain were measured. For acute studies, rats were injected intravenously with lead acetate (2 and 5 mg/kg) and ICP/MAP was recorded for 45 min. Selective blockers were administered prior to lead to investigate its mechanism of toxic action. **Results:** Subchronic treatment with lead acetate 0.5 and 2 mg/kg significantly reduced erectile responses over the range of 0.5-10 Hz. At 1 Hz, ICP/MAP was reduced to 0.161  $\pm$  0.037 and 0.089  $\pm$  0.001 by the action of 0.5 and 2 mg/kg lead acetate respectively, compared to 0.296  $\pm$  0.053 as control. This was associated with a significant elevation of malonaldehyde level and reduction of nitrite/nitrate level in corpus cavernosum. No change was observed on brain parameters excluding centrally-mediated effects for lead in the tested doses on sexual functions. In acute studies, lead acetate (2 and 5 mg/kg) reduced neurogenic erections by 28.42  $\pm$  3.76% and 96.84  $\pm$  8.52% respectively with maximum effect being attained 30 min after injection. No significant effect on blood pressure was observed. The anti-erectile effect of lead was masked in the presence of nitric oxide synthase inhibitor (L-NNA) or potassium channel blocker (TEA) or guanylate cyclase inhibitor (methylene blue) but not in the presence of hemoxygenase inhibitor (ZnPP). Vitamin C, but not sildenafil, reversed the inhibitory effect of lead on erection. **Conclusion:** Lead acetate may inhibit erectile process in rats. It seems that lead, besides its pro-oxidant effect and consequent inactivation of nitric oxide, negatively modulates the action of nitric oxide on guanylate cyclase and potassium channels.

#### 154. Exposure of Healthcare Workers to Platinum Salts during a Heated Intraperitoneal Perioperative Chemotherapy Procedure

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**Objective:** Heated Intraperitoneal Chemotherapy (HIPEC) is a promising new therapy for peritoneal carcinomatosis. However, it can potentially expose healthcare workers to cytotoxic agents, during both the operative and postoperative phases. **Methods:** This study assessed external exposure to oxaliplatin and internal contamination of healthcare workers in two different operating rooms during 3 successive HIPEC procedures in each site. Exposure was assessed by measuring platinum (Pt): 1) in air (individual and environmental samples), 2) on various surfaces (including the operating table, the operating room floor, shoe covers, shoes, gloves, and healthcare workers' hands), 3) urine samples from medical staff. Pt concentrations were determined by inductively coupled plasma mass spectrometry. **Results:** Pt was not detected in the air of the operating room. Minor surface contamination of the operating table, the floor in front of the surgeon, shoe covers and shoes was observed. The operating surgeon's outer gloves were heavily contaminated. The inner gloves and the surgeon's hands were also slightly contaminated when the surgeon used double gloves only, but not when he used triple gloves. Urine Pt was undetectable (< 5 ng/L) in most exposed workers (44), but was detectable although not measurable (< 16 ng/L) in 4 workers. **Conclusion:** This study indicates a low risk of systemic contamination with platinum salts for healthcare workers in operating rooms during HIPEC procedures. The routine use of triple gloves by surgeons and double gloves by nurses is recommended for prevention of hand contamination during all procedures involving cytotoxic agents. Surgeons in direct contact with chemotherapy should also use outer gloves up to the elbow. The surgeon's gloves should be changed every 30 minutes during the HIPEC procedure. At the end of the HIPEC procedure, prolonged washing of hands with soap and water is mandatory for surgeons and nurses.

#### 155. Discovery of an Epidemic of Lead Poisoning in Children in a Shantytown in Reunion Island

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**Objective:** Reunion Island is a French overseas department in the Indian Ocean where the problem of childhood lead poisoning was considered as insignificant compared to mainland France, as the habitat is relatively recent and does not contain old lead contaminated paints. In March 2009 during a national survey for detection of lead impact in childhood, the lead blood level (LBL) of a young boy from a shantytown of one city in the suburb of Saint Denis called "le Port" was surprisingly high (140

µg/L). His 5 brothers and sisters were tested with high LBL also. The origin of the lead was unclear: no contaminated paint, water or dust in the house. An environmental survey was performed with the discovery in the shantytown of traffic in car batteries with heavy metal soil contamination. As soon as the lead origin was determined an evaluation of childhood lead impregnation in the poor suburb was proposed. **Methods:** An information campaign in the Island was carried out in order to alert the general practitioners, the educational system and the shantytown families themselves. The local authorities took a census of the concerned population with 87 families and about 300 people. The aim was to obtain for all the children living in the contaminated area an LBL evaluation. **Results:** During the 18 months study (from 01/01/2010 to 30/06/2011), 113 children from the shantytown were tested (average age 7 years, 59 boys/54 girls). Eighty-eight of them had an LBL up to 50 µg/L, including 58 of them with LBL up to 100 µg/L (official limit in France to declare a case of child lead poisoning; maximum observed 387 µg/L). In order to complete the study, blood samples were also performed in 16 adults from the shantytown showing no contamination. All the lead poisoned children were medically managed with evaluation of lead impacts like anaemia, cognitive disturbances or digestive troubles. **Conclusion:** After this study rehousing of the 87 shantytown families was performed and the soil was decontaminated. Information in the local media about the dangers of heavy metals for children was also disseminated to avoid similar traffic elsewhere.

#### 156. Life-Threatening Methemoglobinemia Induced by Vehicle Exhaust Fumes in a Suicide Attempt

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**Case report:** A 47 year Caucasian depressive female was found comatose in her car, six hours after a suicide attempt with drugs and inhalation of automobile exhaust fumes (hose from the engine to the interior of the vehicle). Clinical examination showed coma CGS 6/15, myosis, dyspnoea with deep cyanosis of lips and extremities. BP was 145/92 mmHg, HR 104 bpm, SpO<sub>2</sub> 89%. ECG was normal. Temp was 36.2°C. Dextrose was 6.4 mmol/L. She was intubated with mechanical ventilation. End tidal carbon dioxide (ETCO<sub>2</sub>) was 33 mmHg. Cyanosis was persistent despite normobaric oxygenation. First ABG showed pH 7.28, PO<sub>2</sub> 358 mmHg, PCO<sub>2</sub> 35 mmHg, SpO<sub>2</sub> 87%, HCO<sub>3</sub> 16 mmol/L, lactate 3 mmol/L, carboxyhemoglobinemia 1.5% and methemoglobinemia was 33.5%. Hepatic, cardiac, renal biology were and stayed unremarkable. HPLC wide screening showed zopiclone level 158 microgram/L (3 times normal), acetaminophen 45 milligram/L. Methylene blue was given in a 1 mg/kg dose associated with the usual N-acetylcysteine antidotal regimen by intravenous route. She was observed in the Intensive Care Unit with 3 days mechanical ventilation and discharged on Day 7. Methemoglobinemia (MHb) is rarely observed (357/1,058,783) in poisoning cases from French Poison Centers Database (during the years 1999–2008). 74.5% of these 357 cases were due to well known methemoglobinising agents e.g. nitrates, sodium

chlorate, fertilizer. Acetaminophen (P.phenetidin), and zopiclone are known to cause this in very few cases. Acetaminophen was eliminated here (low level, no hepatic disturbances). Ingestion of 100 tablets of zopiclone can produce Mthb. Automobile catalytic converters produce azote oxides (NOx) with 90% NO, 10% NO<sub>2</sub>, carbon dioxide and low carbon monoxide; even with low engine regime. Diesel engines produce 3 folds more NOx than gasoline powered. NO<sub>2</sub> is toxic for haemoglobin and produces Mthb (Kosaka equation). Three Mthb forensic cases due to gas exhaust inhalation have been published. **Conclusion:** Azote oxides from engine exhaust fumes can produce severe Mthb in suicide exposures. **References:** 1. Clissold SP. Paracetamol and phenacetin. *Drugs* 1986; 32:46–9. 2. Fung HT, Lai CH, Wong OF, et al Two cases of methemoglobinemia following zopiclone. *Clin Toxicol (Phila)* 2008; 46:167–70. 3. Vevelstad M, Morild I. Lethal methemoglobinemia and automobile exhaust inhalation. *Forensic Sci Int* 2009; 187:e1–5.

#### 157. Risk Factors for Carbon Monoxide Poisoning in Fez

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**Objective:** In Morocco, poisoning with carbon monoxide (CO) is still common, serious and often unrecognized. It is a public health problem. The present retrospective study aimed to describe the epidemiology, clinical features and outcome of all cases related to carbon monoxide poisoning occurring between January 2009 and June 2011 in the region of Fez-Boulmane. **Methods:** The data were collected from the medical records of patients who consulted one of five hospitals in the region. The demographic features, circumstances, symptomatology and outcome were analyzed. The patient's clinical state was classified according to the Poisoning Severity Score "PSS", and IPCS age groups were used. Univariate analysis was conducted to identify factors associated with severity. **Results:** In our study, we collected 1141 cases of carbon monoxide poisoning. The mean age was 21.08 ± 15.30 years. The adult age group was more common. The sex ratio (male/female) was 0.4 in favour of female. Pulmonary route was involved in 100% of cases and domestic use represented 86.2%. The circumstance of poisoning was accidental in 99% of cases. The phenomenon of CO poisoning showed a seasonal pattern with winter and fall exacerbation (70%). Poisonings by CO were concentrated in the region of Fez (61.4%) followed by the region of Sefrou (24.7%) and Missouri (6.9%). Symptomatology was represented by neurological signs in 57.3% with dizziness in 20.7% and headache in 18.4% of cases, followed by gastrointestinal symptoms in 22.9%. Respiratory signs were found in 17%. The lethality rate was 1.05%. Univariate analysis comparing the groups of severe poisoning and non-serious has shown that sex ( $p = 10^{-3}$ ), seasons ( $p = 10^{-3}$ ), some clinical signs (nausea with  $p = 0.0001$  and headache with  $p = 0.0009$ ), and rural origin of intoxication significantly influence the severity of patients. **Conclusion:** Carbon monoxide poisoning is frequent and severe. Patients and health professionals should be aware of the potential dangers of such poisoning in order to prevent or limit the consequences.

**158. Barbecues – An Unusual Cause of Carbon Monoxide Exposure Reported to the UK National Poisons Information Service 2010–2011**

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**Objective:** Carbon monoxide (CO) is a colourless and odourless poisonous gas formed from the incomplete combustion of substances containing carbon (fossil fuels). The majority of the reported cases are due to smoke inhalation occurring in house fires or faulty appliances. In the UK, more than 50 people die from accidental carbon monoxide poisoning every year, and 200 people are seriously injured. However, due to the unspecific nature of symptoms, undiagnosed cases could be much higher. A great deal of revenue is spent on CO exposure prevention, although these tend to focus on faulty domestic appliances. Significant exposure to CO can also result from other sources. **Methods:** Calls reported to the UK National Poisons Information Service (UK NPIS) during 2010–2011 were analysed, focusing on exposures that did not originate from domestic appliances or house fires. **Results:** In 2010/2011 there were 286 carbon monoxide related enquiries to the NPIS (NPIS annual report) involving at least 385 patients. While the majority of cases (64%) were regarding CO exposure from domestic appliances and 19% came from domestic fires, there were a number of interesting cases that resulted in raised carboxyhaemoglobin levels from other sources. Noticeable was the increased number of CO exposure originating from barbecues being brought into enclosed areas such as homes or tents. There were five enquiries involving ten patients during this time that resulted from inhalation of fumes from a barbecue; all resulted in symptoms and most had raised carboxyhaemoglobin levels recorded. There was one fatality that resulted from intentional inhalation of fumes from several barbecues in an enclosed space. **Conclusion:** Recently there have been several media-reported carbon monoxide fatalities from people moving barbecues into tents. It is quite obvious from our data that although this type of exposure is rare it is not isolated and can lead to severe morbidity and in some cases fatalities. This type of exposure is not specifically mentioned in the document from the department of health PL/CMO/2010/02 that is aimed at increasing public awareness of carbon monoxide poisoning. We recommend that the public should be made aware that outdoor activities, like barbecues, can cause significant CO exposure.

**159. Agitated Delirium and Risk of Adverse Cardiovascular Events Following Acute Overdose**

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**Objective:** Agitated delirium (AD) is common in acute overdose patients. Risk factors for adverse cardiovascular events (ACVE) in overdosed emergency department (ED) patients have previously been derived, but the relationship between AD and risk of ACVE remains unknown. This study characterizes

the relationship between in-hospital ACVE in ED patients who present with AD following acute overdose. **Methods:** This prospective cohort study enrolled consecutive adult (> 18 years) ED patients with acute overdose in one urban, tertiary care hospital over 14 months (2009–2010). Subjects with AD (defined as specific ED chart documentation of “agitation” requiring chemical sedation) were prospectively followed to hospital discharge and data was abstracted from the medical record. In-hospital ACVE was defined as the occurrence of  $\geq 1$  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). **Results:** There were 391 ED patients with suspected overdose screened, of whom 108 (28%) patients met criteria for AD (mean age 40.1, 58% male, 3.7% mortality). The most frequent exposures were ethanol co-ingestion (25) and cocaine (14). Laboratory analysis revealed mean creatine phosphokinase (CPK) 3,435 (units/liter) and mean lactate 3.1 (mmol/L). For sedation, 65 patients received an antipsychotic alone and 43 received a benzodiazepine either alone or in combination with an antipsychotic. During the study period, there were 8 (7.4%) ACVE. Factors associated with ACVE were lower serum ethanol concentration (t-test  $p < 0.001$ ) and younger age (t-test  $p < 0.01$ ), while non-significant factors included sedative drug, cocaine, CPK, and lactate (p all NS). In the ethanol-negative subgroup (N = 66), sedative choice remained a non-significant predictor of outcome. **Conclusion:** AD is a common presentation for ED patients with acute drug overdose, and ACVE in this group appears to be consequential. Predictors of ACVE were low serum ethanol concentration and younger age. Sedative agent choice was not associated with outcomes. Implications for the management of AD following acute drug overdose require further study with regard to optimization of adverse event mitigation.

**160. Easily Available Highly Poisonous Drain Cleaners: Three Case Reports of Ingestion**

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**Objective:** Drain cleaners are usually strongly alkaline or strongly acidic corrosive solutions. Ingestion of corrosives can lead to extensive damage to the gastrointestinal tract and serious systemic features that may lead to death. Late complications may include stricture formation, gastric outlet obstruction and oesophageal carcinoma. We present 3 cases of serious drain cleaner ingestions which happened within a short period of time. **Case series:** Patient 1, a 37 year old male, presented at the emergency department (ED) 20 minutes after ingesting 1–2 sips of a drain cleaner (> 90% sulphuric acid) in a suicide attempt. He was intubated and received standard supportive care in the intensive care unit (ICU) but went into cardiac arrest and died 6 hours after the ingestion. Patient 2, a 39 year old male, presented at ED shortly after he was given a drink in a party contaminated with a drain cleaner (96% sulphuric acid). He was intubated and received steroids, antibiotics and standard supportive care in ICU. He was discharged from hospital after 2 weeks but developed oesophageal strictures, severe depression, anxiety and sleeping problems. Patient 3, a 66 year old

male, grabbed a bottle of drain cleaner (30% sodium hydroxide) in a hardware store and drank in a suicide attempt. He presented to ED within half an hour of the ingestion. He was intubated and admitted to ICU. He had episodes of atrial fibrillation, repeated pneumonia, pulmonary collapse and respiratory failure and died 7 weeks later. **Conclusion:** Corrosive drain cleaners are easily accessible and highly poisonous solutions where one sip can kill. Treatment is very difficult and requires expensive care in ICU and the survivors may suffer from lifelong complications. The first case got extensive media coverage which raises the question whether the resemblance of the cases that happened within a short period of time was a coincidence. These cases highlight a fatal mode of self-poisoning and malicious intentional poisoning that might be controlled through restriction of sales and limitations of access.

**161. Reaction of the Amine Precursor Uptake and Decarboxylation System during Acute Chemical Trauma**

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**Objective:** The study was proposed to determine the response of amine precursor uptake and decarboxylation (APUD) system peptides on acute chemical trauma caused by corrosive substances (ACTCS). **Methods:** Twenty-four patients with ACTCS underwent radioimmunological study of blood contents of neurotensin (N), substance P (SP) and vasoactive intestinal polypeptide (VIP). Blood samples were taken at hospital admission (within 1.5 hours after injury), and thereafter at 4th, 12th and 24th hours subsequently. Healthy volunteers' N, SP and VIP contents were estimated as 100%. **Results:** N concentration was increased to 282% at hospital admission, enhanced to 435% at 4th hour, maintained at this level at 12th hour and decreased to 207% after 24 hours. SP was increased up to 615% at submission, sustained at this level till 12th hour and reduced to 370% at 24th hour. VIP at admission was 170%, augmented to 275% at 4th hour and thereafter diminished gradually to 250 and 230% respectively at 12th and 24th hours. **Conclusion:** The listed substances are known to induce vasoconstriction and their increase would be evaluated as a body compensatory response to acute chemical injury. Along with the Renin-Angiotensin-Aldosterone system they deal with hypovolemia and hypotension caused by chemical trauma. Very high contents of SP could be explained due to its participation in pain medication.

**162. Dose Adjustment of Trivalent Equine Antitoxin in the Treatment of Infant Botulism**

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**Objective:** Infant botulism (IB) results from absorption of neurotoxins produced *in situ* by *Clostridia* coloniz-

ing the intestinal lumen in infants aged less than one-year. Currently, different antitoxin formulations are available and administered in different doses in IB in Italy, Argentina and US. In Italy and Europe, a 500 mL standard dose of a Trivalent-Equine-Antitoxin (TEqA) (750 IU-anti-A, 500 IU-anti-B, 50 IU-anti-E per mL) is registered for all the botulism forms. US-FDA licensed the intravenous Human-derived Immune-Globulin preparation (at least 15 IU-anti-A, 2 IU-anti-B per mL) at the dose of 2 mL/kg for IB; a Bivalent-Equine-Antitoxin (750 IU-anti-A, 550 IU-anti-B per mL) is used in IB in Argentina at the dose of 0.66 mL/kg. The antidote type and the appropriate dose for IB are thus not yet internationally standardized. We report two recent cases of IB in which two different doses of TEqA were administered trying to assess the minimal effective dose. *Case series:* Among the cases of IB referred to the Pavia Poison Centre in 2009–2011, two cases in which TEqA was administered were included. Case 1. A 3-month-old male (5 kg body weight) presenting acute abdominal pain underwent urgent explorative laparotomy that excluded volvulus; 24 hours later, mydriasis and diffuse hypotonia appeared, requiring endotracheal intubation. *C. botulinum* (enema) and toxin type-B (enema and serum) were detected. TEqA (125 mL) was administered intravenously. Case 2. A 7-month-old male (7 kg body weight) presented with a 7-day history of stipsis, ptosis, mydriasis, drowsiness, weak cry, urinary retention and floppiness. *C. botulinum* and toxin type-B were detected in stools. TEqA (75 mL) was administered intravenously. Transient erythematous-rash appeared. Both babies fully recovered. *Conclusion:* IB remains a rare disease, and in selected cases may require an antidote. In both our cases TEqA did not cause serious adverse reactions and improved the clinical picture. The optimal dose probably should be related to the circulating toxin levels, which in IB is known to be low: in our cases 10–25 mL/kg of TEqA (less than the producer recommended dose) was effective, but remain larger than those used in Argentina and US. A further reduction is probably needed.

### 163. A Case of Adult Botulism Secondary to a Psychiatric Illness

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*Objective:* Botulism predominately affects adults when they ingest pre-formed toxin. The majority of these outbreaks result from faulty home processing of food or high-risk cultural or religious food practices of various ethnic groups. Although there have been several cases tied to non-cultural unusual food practices, none are documented secondary to mental illness. We present an adult male who developed botulism by unsanitary food practices secondary to his schizoaffective disorder. *Case report:* A 59 year old man with a history of schizoaffective disorder complained of difficulty speaking for 6 hours. Symptoms rapidly progressed to difficulty swallowing and the patient was intubated secondary to inability to handle secretions. A bulbar palsy was noted at that time. A non-contrast head CT and a lumbar puncture were normal. Over the next 24 hours, the patient developed proximal weakness. Botulism anti-toxin was administered 36 hours after presentation. Evaluation of the patient's home by the Department of Health revealed odd food storing and preparation practices. The patient had a history of prior food borne illnesses and a social worker had been working with him to develop more sanitary food practices. The refrigerator temperature

was 15.6 centigrade and food was mixed and stored in open pots that were left on counter tops for unknown periods of time. Mice assay and PCR of gastric contents confirmed Botulism type A. A sauce in a pot from the stove and a cheese and barley mixture from the house tested also positive for Botulism type A. One month post-exposure, the patient could not open his eyes, was still ventilator-dependent and was only moving his fingers and toes. *Conclusion:* Although botulism is rare in the US, certain groups such as native Alaskans and injection drug users are known to be at increased risk. This case of adult food borne botulism is unusual in that a psychiatric illness led to unsanitary food handling behaviors and subsequent botulism growth in un-canned food. Clinicians should have a high suspicion for botulism in any patient who presents with new onset bulbar palsies. Careful questioning and examination should be performed to ensure prompt delivery of antitoxin.

### 164. Acute Poisoning with a Lethal Dose of Cupric Sulfate: Atypical Presentation

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*Objective:* Copper sulfate is still widely used as a fungicide. Acute copper sulfate poisonings are comparatively rare. They are usually accidental after unintentional intake of an aqueous solution, containing cupric sulfate with vague clinical signs, mainly from the gastrointestinal system. Intentional intake may cause severe poisonings as a result of the strong oxidative and corrosive properties of copper sulfate. *Case report:* We present a suicidal poisoning with 60 grams cupric sulfate, dry crystalline substance, in a 47 year old woman with long lasting depression. She was hospitalized 4 hours later with symptoms of toxic gastroenteritis – multiple vomiting and diarrhea. Hemolytic syndrome developed gradually on day 3, reaching its maximal intensity on days 4–5. Clinical presentation included dizziness, icterus, dark red-brown urine and corresponding laboratory abnormalities – free hemoglobin 65 milligram% ( $\leq 2$  milligram%), indirect bilirubin 220.7 micromol/L (3.4–21.0), hemoglobin 65 grams/L (120–160), erythrocytes 2.2 T/L (4.2–5.4). Gastroscopy revealed only mild irritant lesions. Diuresis remained adequate to fluids during the entire poisoning until recovery. Treatment included: decontamination of the gastrointestinal tract, IV infusions up to 4 L/24 hours, steroids, diuretics, H2 blockers, antibiotics, transfusion of erythrocytes and fresh frozen plasma. No antidote was used for managing this potentially lethal poisoning as such was not available in the country at that time. Gradually the patient's condition stabilized. Towards the end of the hospital stay we observed non significant elevation of liver enzymes – AST 97 U/L ( $< 31$ ) and ALT 122 U/L ( $< 34$ ). On day 10 post ingestion the subject was discharged healthy. *Conclusion:* In the course of this severe poisoning the following peculiarities were observed: 1) Late onset of hemolytic syndrome (3–4 days post ingestion); 2) Normal renal function without any signs of acute renal failure (renal function was closely monitored during course of poisoning); 3) Only mild irritant lesions of the gastrointestinal tract; 4) Favorable outcome after severe intoxication with a lethal dose of copper sulfate, despite lack of antidote treatment. We consider the use of large volumes of infusions and diuretics for prevention of renal failure, as well as steroids and substitution with bio-products as an adequate model of therapeutic measures in case of lack of antidotes.

### 165. Cyanide Poisoning from Chronic Ingestion of an Amygdalin Containing Herbal Preparation

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*Objective:* We describe a case report of a patient who had toxicologically confirmed cyanide poisoning associated with chronic ingestion of an amygdalin containing herbal preparation. *Case report:* A 63 year old female presented with dyspnoea and cough potentially due to pneumonia. Past medical history included metastatic carcinoma of the lung, recent pulmonary embolism and she was previously a smoker. Clinical examination demonstrated tachycardia (heart rate: 144 bpm) and hyperventilation (36 breaths/minute) with an oxygen saturation of 97% on 15 L/min oxygen. Arterial pH was 7.44, base excess -11.7 and plasma lactate 11 mmol/L. Hepatic and renal function were normal. The patient reported taking a Mexican herbal product called Novodalín (amygdalin B17 extract 500 mg, apricot powder) over 5 months as a cancer remedy. Blood cyanide concentration was measured as 4.38 mg/L. The patient was treated with intravenous sodium thiosulphate and fluids together with antibiotics and corticosteroids. By the 5th day of hospitalisation arterial pH was 7.49, base excess -2.6 and lactate 2.3. Cyanide concentration on the fifth day of presentation was 0.14 mg/L. Oxygen requirements remained high, possibly due to her underlying lung condition, but she remained haemodynamically stable. *Conclusion:* This case demonstrates elevated blood cyanide concentrations associated with clinical and biochemical features of cyanide poisoning after chronic use of this herbal preparation, although this episode was complicated by significant underlying respiratory co-morbidity. Apricot kernels contain amygdalin, a cyanogenic glycoside synthesised in over 100 families of flowering plants.<sup>1</sup> When the kernels are chewed an endogenous  $\beta$ -glucosidase enzyme (emulsin) catalyses the hydrolysis of amygdalin to hydrocyanic acid (HCN) and there are case reports of cyanide toxicity following apricot kernel ingestion.<sup>2</sup> Cyanogenic compounds have been used as antineoplastic therapy, but their efficacy remains unproven.<sup>3</sup> *References:* 1. Francisco IA, Pinotti MHP. Cyanogenic glycosides in plants. *Braz Arch Biol Technol* 2000; 43:487–92. 2. Akyıldız BN, Kurtoğlu S, Kondolot M, et al. Cyanide poisoning caused by ingestion of apricot seeds. *Ann Trop Paediatr* 2010; 30:39–43. 3. Milazzo S, Lejeune S, Ernst E. Laetrile for cancer: A systematic review of the clinical evidence. *Support Care Cancer* 2007; 15:583–95.

### 166. Abuse of Ethyl Alcohol-Containing Hand Sanitizer (Including Inpatient Ingestions) Associated with Venous Sinus Thrombosis

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*Objective:* Alcohol-based hand rubs (AHR) are ubiquitous in health care facilities; common formulations contain 70% ethyl alcohol. Human ingestions of AHRs have been reported.<sup>1,2</sup> This case is unique in terms of recidivism (12 AHR ingestions) involving ingestions occurring in emergency departments (EDs) and behavioral health facilities (BHF). *Case report:* A 37-year-old man with a history of ethanol abuse, ethanol withdrawal

seizures and bipolar disorder, was called to our poison control center after an intentional ingestion of AHR. He was inebriated and tachycardic (HR = 114) but otherwise had a normal examination. Serum ethanol concentration (SEC) was 323 mg/dL. He was monitored, received IV fluids and then transferred to a BHF. Several months later, a subsequent AHR ingestion resulted in a SEC of 295 mg/dL. Within 24 hours of presentation, and after admission to a BHF, he developed headache and scotoma, followed by syncope. Head CT revealed acute venous sinus thrombosis (VST) with hemorrhagic conversion. He was anticoagulated after failed thrombectomy. Neurological consultation suggested dehydration secondary to substance abuse as the etiology. Over a ten month period, this patient had 15 ED evaluations related to ethanol abuse, including 12 AHR ingestions. Six AHR ingestions occurred in an ED and two occurred in a BHF. One incident started with an AHR ingestion from a BHF dispenser and then, hours later, a second ingestion from an ED dispenser. The average SEC for all ED visits was 239 mg/dL (range: 58–418; n = 14). **Conclusion:** This case describes a patient with 12 separate ingestions of alcohol-containing hand rub resulting in hospital admissions and neurologic morbidity. Since several ingestions occurred as an inpatient, health care facilities must recognize the potential for abuse of these dispensers. We hypothesize that chronic abuse of alcohol (via a sanitizing agent) was associated with the development of venous sinus thrombosis. **References:** 1. Archer JRH, Wood DM, Tizzard Z, et al. Alcohol hand rubs: hygiene and hazard. *BMJ* 2007; 335:1154–5. 2. Henry-Lagarigue M, Charbonnier M, Bruneel F, et al. Severe alcohol hand rub overdose inducing coma, watch after H1N1 pandemic. *Neurocrit Care* 2010; 12:400–2.

### 167. Radioactive Strontium Poisoning: A Memory of World War II

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**Objective:** To report a case of poisoning with strontium. **Case report:** A 43 year-old man, with a history of chronic alcoholism, found a thick, transparent capsule in the sand on a beach on Oleron Island, France. He broke the capsule and mixed the yellow powder with a glass of white wine. After about 30 minutes he felt a retrosternal burn and headache and called the first aid service. On the capsule was written "radioactive p ison inside US Rad M Corp Bury if damaged". After some research this capsule was found to be used during WW2 to help American planes to land on this island by night. Two hours after the intake a first dosimetric analysis showed 28 to 80 mRad/h on the chest of the patient. Skin decontamination was then carried out, and the radioactivity declined to 0.5 mRad/h after the procedure. The capsule showed 40 mRad/h and was buried. On admission to the closest Hospital Emergency Room the patient presented the same symptoms, with an ethanol blood level of 2.2 g/L. After advice from the Bordeaux Poison Center (PCC) he was given 15 g of sodium alginate and repeat skin decontamination was performed. He was then sent to Bordeaux University Hospital. On admission to the intensive care unit (ICU) he remained dizzy, with retrosternal burning sensation and wheezing. A new measurement was performed showing an external radiation of one shock/second on the chest. After a third decontamination, we gave him 10 grams of sodium alginate which was then sucked back. Several blood, urine and stool samples were taken to measure radioactivity. Hemogram was always strictly normal.

Dosimetric analyses showed that the capsule contained a 100 microCurie dose. The supposed ingested dose was 30 microCurie, and 60% of the dose was eliminated in stools in the first 48 h. The dose actually absorbed was estimated at 10 microCurie, that is 3.7 French Public Annual Incorporation Limit (5 mSv) = 18.5 mSv. The patient was released home ten days after the accident. He was then lost to follow-up. **Conclusion:** This exceptional case report shows that nuclear plants are not the sole possibility for radioactive accidents.

### 168. Lethal Ingestion of a Maximum of 4.5 Seeds of *Ricinus communis* in a Dog

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**Objective:** *Ricinus communis* (castor bean plant) contains the toxalbumin ricin which is a potent inhibitor of protein synthesis and can cause cell death. When the seeds or other plant materials are chewed and swallowed, ricin can easily be absorbed from the gastrointestinal tract and cause severe symptoms and death.<sup>1</sup> In most intoxications previously published, the ingested amount is not reported, but in our case the exact amount ingested is specified. **Case report:** Drever, bitch, 7 years old, 12.5 kg, consumed 3.5 or 4.5 seeds of *Ricinus communis*. Five or six seeds were newly planted in a pot. The dog ate the seeds from the pot in the afternoon and only 1.5 seeds were found afterwards. The next morning she vomited several times and was shivering. The bitch was taken to the veterinary clinic. The general condition was moderately impaired. Normal temperature, 38 degrees centigrade and tachycardia 200 bpm. Charcoal orally, fluid IV, ranitidine SC and sucralfate orally were given. She vomited repeatedly during the afternoon. Day 3 the general condition worsened with haematuria, melaena, bloody diarrhoea, temp. 36 degrees centigrade, tachycardia 200 bpm and weak pulse. Capillary refill time was seriously prolonged and she had pale mucous membranes. Symptomatic treatment with fluid IV, plasma IV, vitamin K1 IM, tranexamic acid IV, sucralfate orally and ranitidine SC were given. Serum albumin was very low (6 g/L), APTT prolonged (147 sec.) and there was an elevated creatinine (175 micromoles/L). The bitch died in the afternoon approximately 48 hours after ingestion. No autopsy was performed. **Conclusion:** There is no specific treatment or antidote for ricin intoxication. In this case the ingested amount of ricin seeds was known, a quantity proved to be lethal. **Reference:** 1. Soto-Blanco B, Sinhorini IL, Gorniak SL, et al. *Ricinus communis* cake poisoning in a dog. *Vet Hum Toxicol* 2002; 44:155–6.

### 169. Oral Desmopressin Overdose in a Young Child

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**Objective:** To report a case of oral desmopressin overdose in a young child. **Case report:** A two year old healthy toddler was referred to the emergency department one hour after ingesting 15–18 0.2 mg desmopressin tablets, 3–3.6 mg or 0.27–0.32 mg/kg in total. She was witnessed holding an open bottle of desmopressin tablets with powder in her mouth. The ingested amount was estimated by pill count. On admission she was

asymptomatic. Physical examination was unremarkable; pulse 100/minute, blood pressure 100/78 mmHg, rectal temperature 36.7 degrees centigrade, respiratory rate 20/minute, oxygen saturation 99% in room air. Serum sodium was 141 mEq/L, serum potassium 4.9 mEq/L, serum osmolality was 283 mOsm/kg water. Blood urea nitrogen (BUN) and creatinine were in the normal range. Urine sodium was 222 mEq/L and urine osmolality 546 mOsm/kg water. The child was admitted for 12 hours' observation during which she remained asymptomatic and passed urine. Repeated neurological and ophthalmological examinations excluded increased intracranial pressure. Laboratory evaluation before discharge revealed minor changes in serum electrolytes and osmolality; sodium decreased to 138 mEq/L, potassium to 3.9 mEq/L, and serum osmolality to 277 mOsm/kg water. BUN and creatinine remained normal. Urine osmolality increased to 832 mOsm/kg water and urine sodium increased to 333 mEq/L. **Conclusion:** Acute ingestion of 0.27–0.32 mg/kg desmopressin in a two year old child did not result in any adverse clinical effect. To our knowledge, this is the first report of an oral desmopressin overdose in a young child. Published cases report only unsupervised use of the nasal formulation of the drug by children aged 6 years or higher. Based on desmopressin pharmacokinetic data, the laboratory results obtained in our patient after 12 hours may represent the tail end of its antidiuretic effect. It is suggested that serum and urine electrolytes and osmolality be determined four to six hours after ingestion of desmopressin in order to detect its maximal effect.

### 170. Bi-Modal Dialysis and Surgery: Two Alternatives in Extreme Hyperkalemia

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**Objective:** To report a case of extreme hyperkalemia requiring more than standard medical treatment. Severe poisoning with potassium pills is rare but patients may present with severe cardiovascular symptoms requiring immediate and effective treatment. **Case report:** A 30 year-old healthy but mentally depressed woman presented to the emergency department (ED) after ingestion of 300 slow-release pills of potassium chloride, adding up to 225 g of potassium. She was brought to the ED with a serum potassium of 9.5 mmol/L. She was hardly awake, with a blood pressure of 60/35 mm Hg, and poor cardiovascular function. She soon developed ventricular fibrillation that resolved instantly by rapid intravenous administration of 72 mg calcium chloride. No electrical cardioversions were needed. Gastric lavage was performed in the intensive care unit (ICU) after an x-ray revealed large amounts of tablets in the stomach. She received intensive medical treatment with glucose/insulin, salbutamol, sodium bicarbonate and resonium, serum potassium was 8.5 mmol/L. Venovenous haemodialysis was initiated with serum potassium at 8.4, and despite ongoing dialysis potassium increased to 10.3 mmol/L. Hence a parallel continuous renal replacement therapy (CRRT) was started via another central dialysis catheter. After one hour of double dialysis, serum potassium decreased to 9.2 mmol/L. An x-ray revealed large amounts of pills in the GI-tract and the patient was taken to the operating theatre with ongoing CRRT. The surgeon was able to successfully remove about 200 pills through a laparotomy. Serum potassium thereafter soon dropped to 5.2 mmol/L. The patient recovered slowly after seven

days in the ICU, but later developed a gastric stricture. *Discussion:* Potassium poisoning with slow-release preparations poses an extra high risk for therapy-resistant hyperkalemia. Both dialysis and surgery have been used previously, but we have found no other case where bi-modal dialysis has been attempted. In this case bi-modal dialysis increased the effectiveness of dialysis and decreased potassium values to non-life-threatening levels and surgery prevented further absorption of potassium. *Conclusion:* Parallel bi-modal dialysis, as well as surgery present alternatives for therapy-resistant hyperkalemia in potassium poisoning. Standard veno-venous haemodialysis may be insufficient, but the addition of continuous CRRT resolved this very dramatic case.

### 171. Irreversible Alopecia Consequent to Hypervitaminosis A and Hypercarotenodermia

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<sup>2</sup>Poison Control Center, IRCCS Fondazione Maugeri and University of Pavia, Italy

*Objective:* Hypervitaminosis A is a well described clinical entity usually observed after ingestion of large amounts of vitamin A. Hypercarotenodermia is a yellow discoloration of the skin due to the deposit of beta-carotene in the stratum corneum. We report a case of clinically manifested hypervitaminosis A associated with hypercarotenodermia, following the chronic ingestion of vitamin A supplements and vegetables containing high quantities of beta-carotene. *Case report:* An alternative physician prescribed to a 46-year-old female complementary medicines and food rich of vitamin A because of visual disturbances and as an antioxidant. The patient began therapy with 25,000 IU of vitamin A and carrot juice for six months; then, she added complementary medicines with beta-carotene and tablets of myrtillus containing 15 mg of beta-carotene each for twelve months. Estimates of her vitamin A and carotenoid intake, based on daily consumption of carrot juice and medicines, ranged from 25,000 up to 205,000 IU daily for a period of eighteen months. She progressively developed a chronic vitamin A intoxication syndrome: main complaints included myalgias, pains in bones and joints, oligomenorrhea, exfoliative dermatitis and alopecia. Diagnosis was not conclusive until she presented to the emergency department with a yellow coloration of her skin when diagnosis of vitamin A intoxication was made. Drugs and supplements as well as carrot juice were stopped after the diagnosis. Fourteen months later, all clinical symptoms except alopecia had improved. Three years after the cessation of vitamin A intake, alopecia was present despite treatment with oral and topical corticosteroids and topical minoxidil. *Conclusion:* Chronic vitamin A toxicity in humans can occur after several months or years of consumption of large amounts (> 30,000 IU for 6 months) of vitamin A. By contrast, hypercarotenodermia is usually a harmless condition. Although 60–70% of dietary beta-carotene is converted to retinol in the human gut, excess of beta-carotene does not cause hypervitaminosis A, due to inhibition of vitamin A production from beta-carotene when dietary intake of beta-carotene is high. In our case, intoxication of vitamin A occurred with relatively small amounts of vitamin A but in association with large amounts of beta-carotene. Alopecia was the only permanent clinical manifestation.

### 172. Fatal Drotaverine Poisoning

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*Objective:* Drotaverine is a synthetic papaverine analogue that has been used since 1965 as an antispasmodic. Drotaverine hydrochloride (No-Spa, Sanofi-Aventis) is available without prescription in the UK. Adult doses are normally 40–80 mg 3–4 times daily by mouth. Emesis, bradycardia, hypotension, and somnolence may occur after overdosage.<sup>1</sup> A 21-year-old woman, said to have ingested 800 mg drotaverine hydrochloride, suffered seizures, hypotension, and cardiac arrest. Although resuscitated, she died of ischaemic brain injury without recovering consciousness.<sup>2</sup> *Case report:* A 19-year-old woman told her flatmates she had taken tablets after talking on the telephone with a boyfriend. She was shaking uncontrollably, and had yellow saliva at the corners of her mouth. She vomited approximately a glass full of yellow liquid after being given water to drink. A bottle that had contained 100 × 40 mg drotaverine hydrochloride tablets was retrieved, 5 tablets remained. An ambulance was called, but before it arrived she was reported as stiffening as if having a fit. She then turned blue, her teeth clenched, she bit her tongue, and her jaw locked. Ninety minutes after presenting to her flatmates, paramedics found her fitting. ECG showed bizarre arrhythmias ranging from extreme tachycardia followed by bradycardia. Twenty minutes later she had a pulseless electrical activity cardiac arrest. After ten minutes spontaneous circulation was restored, but with no respiratory effort. On arrival at hospital she suffered another cardiac arrest from which she could not be resuscitated. Post-mortem examination was inconclusive. Toxicological examination of femoral blood and vitreous humour (both samples in fluoride-oxalate tubes), and stomach contents (total volume not recorded) by TurboFlow™ LC-MS/MS (ThermoFisher Scientific) confirmed the presence of drotaverine at concentrations in blood, vitreous humour, and stomach contents of 0.8, 1.9, and 91 mg/L, respectively. No other drugs were detected during the analysis or on GC-MS screening. *Conclusions:* Drotaverine overdosage may cause vomiting and seizures with associated cardiac toxicity that may prove fatal. *References:* 1. Sentsov VG, Brusin KM, Venichenko NI, et al. Acute drotaverine poisoning. *Clin Toxicol* 2009; 47:456. 2. Culley K, Michels JE, Richardson WH. Fatality following drotaverine overdose. *Clin Toxicol* 2008; 46:615.

### 173. Status Epilepticus from Large Ingestion of Eucalyptus Oil

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*Objective:* Eucalyptus oil is an essential oil derived from natural plant products. There are numerous reports on toxicity from ingestion of eucalyptus oil<sup>1,2</sup> but seizures were reported only in children<sup>3,4</sup>. We report an unusual case of eucalyptus oil poisoning which resulted in recurrent seizures in an adult. *Case report:* A 20 year old lady presented with generalized tonic clonic seizures shortly after the ingestion of an estimated 150 mL of eucalyptus oil. She developed status epilepticus. This did not respond to intravenous diazepam and required intravenous propofol infusion and intubation. Gastric lavage was performed. Other causes of status epilepticus were excluded. She was discharged well with

no neurological sequelae. *Conclusion:* Eucalyptus oil (1,3,3-trimethyl-2-oxabicyclo[2.2.2]-octane) is lipid soluble, it is rapidly absorbed orally, and can be inhaled as a liquid or aerosol. There is little else known about its pharmacodynamics or kinetics.<sup>5</sup> The toxic effect of eucalyptus oil is rapid. Central nervous system involvement includes loss of reflexes and depression of consciousness, which may lead to coma. Seizures can occur but are not frequently reported.<sup>3</sup> Most toxic seizures are short lived and may not require specific intervention. However, for uncontrolled seizure activity, benzodiazepines, then barbiturates and propofol should be used in a stepwise fashion. Decontamination is not recommended due to the risk of vomiting and the potential for rapid onset of seizures and CNS depression. There are no antidotes for this poisoning and there is no evidence to support the use of enhanced elimination techniques like hemodialysis.<sup>1</sup> Our case serves as a reminder of the severe toxic effects of this easily available substance. *References:* 1. Vassallo S. Essential Oils. In: Ford M, Delaney KA, Ling L, et al, eds. *Clinical Toxicology*. 1st ed. Philadelphia, USA: W.B. Saunders Company, 2001:346. 2. Woolf A. Essential oil poisoning. *J Toxicol Clin Toxicol* 1999; 37:721–7. 3. Flaman Z, Pellechia-Clarke S, Bailey B, et al. Unintentional exposure of young children to camphor and eucalyptus oils. *Paediatr Child Health* 2001; 6:80–3. 4. Hindle RC. Eucalyptus oil ingestion. *N Z Med J* 1994; 107:185–6. 5. Eucalyptus Oil (International Programme on Chemical Safety). Available at: <http://www.inchem.org/documents/pims/pharm/pim031.htm>. [accessed 18 Feb 2012].

### 174. Mild Hypoglycaemia and Delayed Effects of Co-Ingestions Following Acute Exenatide (Byetta™) Poisoning

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*Objective:* Exenatide, a glucagon-like peptide-1 (GLP-1) receptor agonist, has been approved as adjunctive therapy to improve glycaemia control in type 2 diabetes. It exhibits many actions of endogenous GLP-1, a gut hormone, which plays a major role in glucose homeostasis by stimulating insulin secretion, suppressing glucagon secretion and inhibiting gastric emptying. Since exenatide acts in a glucose-dependent manner and does not inhibit glucagon release in case of hypoglycaemia, severe hypoglycaemia is not expected during monotherapy. Exenatide maximal blood concentration is obtained 2.1 hours after administration, and the half-life is 2.4 hours. Normal dosing twice daily starts at 5 µg subcutaneously, and can be increased to 10 µg. There is limited information on overdose consequences. Three cases of inadvertent 10-fold higher dose administration were reported during clinical trials. All patients experienced nausea and vomiting, but only one required glucose administration. One previous paper described vomiting without hypoglycaemia after intentional administration of 90 µg. We report one case of overdose involving the highest exenatide dose published so far. *Case report:* A 58-year-old female patient with a history of depression and type 2 diabetes was admitted to hospital after intentional subcutaneous administration of the entire contents (600 µg) of an exenatide pen, combined with the ingestion of levomepromazine (1.2 g) and an unknown amount of clonazepam and zopiclone. Initial findings were unre-

markable, except for nausea. During medical transfer (H+4), finger stick glucose levels decreased from 1 g/L to 0.69 g/L, and quickly rose to 2.8 g/L after 10% dextrose administration. Dextrose was stopped and no hypoglycaemia recurred thereafter. Surprisingly, whereas no impairment of consciousness was noted during the first few hours after ingesting a large amount of psychotropic drugs, the patient became comatose at H+14 and was transferred to the intensive care unit where she required intubation and ventilation (H+16). Her consciousness improved subsequently and she was discharged 2 days later. *Conclusion:* Severe hypoglycaemia is unlikely following exenatide overdose. By inhibiting gastric emptying, it can however result in delayed absorption of co-ingestants, as suggested in this patient by the unexpected delayed onset of CNS symptoms due to psychotropic drug intake.

### 175. Poisoning Cases by Fitness and Wellness Products Sold on the Internet: A European Issue

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*Objective:* Fitness and wellness products sold on the Internet can escape the European dietary food legislation which requires respecting a positive list of ingredients (currently limited to vitamins and minerals), maximum concentrations, traceability and labelling. Often promoted as “safe” and “natural”, some of these products may contain undeclared drugs, impurities associated with plant-based health products or other substances known for their potential side effects. Based on three recent examples, we aim to illustrate the need for systematic analytical assays of these products and collaborations across Europe on this issue. *Methods:* Description of cases registered by the French PCC in 2011. *Results:* 1) A 51 year old woman presented palpitations and dyspnea after consuming “Reduce Weight”, a “natural” appetite-suppressant. Because it may contain an unauthorized drug, sibutramine, an alert was launched by the FDA in 2006. A dose of 22 mg of sibutramine per capsule was found in this case. Afterwards, French authorities discovered a flow of Reduce Weight boxes shipped from Asia. 2) A man aged 23 suffered from rhabdomyolysis after consuming “MASS 3150”, a muscle gaining product. Accountability of the product in this case was finally excluded. However, the product was withdrawn because of the presence of a forbidden plant steroid (*Tribulus terrestris*). 3) A 52 year old man presented palpitations and dyspnea after consuming a fat burner called “Animal Cuts”. According to the website of purchase, this product may contain illegal substances: synephrine and thyroid precursors. Czech and French authorities had previously warned Europe after detection of, respectively, progesterone and excessive concentrations of caffeine. The sale of “Animal Cuts” is currently banned from Internet websites hosted in France. *Conclusion:* Despite the lack of quality assurance for consumers, fitness and wellness products sold on the Internet are widely available, most often without medical advice. These examples highlight the need for systematic assays

in poisoning cases suspected to be associated with such products, and difficulties in trade controls due to the frequent absence of national distributors. A reinforcement of detection, prevention, and public health surveillance of these situations is needed at a European level (e.g. by development of a common database of cases).

### 176. Parenteral Metal Mercury Injection after an Accident with a Thermometer

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*Objective:* To report a case of accidental subcutaneous and muscular injection with metallic mercury without clinical toxic effects after 2 years' follow-up. *Case report:* A 9-year-old girl accidentally fell over a glass thermometer in August 2009, resulting in the injection of the metallic mercury content in the subcutaneous and muscular tissues of her buttock along the right sacral region. A neurosurgical procedure at the time managed to clean up some of the mercury content from tissues, but since the mercury collection was too close to the nervous sheath, the procedure was concluded and some mercury was left in site. Since then the girl is doing fine, with no neurological or neurobehavioral ailments assessed by neuropsychiatric repeated examinations, and neurobehavioral tests. No renal disease has been diagnosed so far. Urine Hg measurements showed a steep decrease through three different periods: 1419.9 µg/gC (Oct/2009); 357.1 µg/gC (Mar/2010); and 51.2 µg/gC (Jul/2011). The last neurological assessment (May/2011) showed no alterations. X-rays and computed tomography showed multiple nodular mercury collection by the right side of L4–L5 vertebrae following the nervous sheath path reaching the upper sacral region. No chelation treatment was carried out, as the girl showed no symptoms or signs of mercury intoxication. *Conclusion:* Differently from elemental mercury being absorbed by inhalation, when Hg<sup>0</sup> rapidly passes the blood-brain barrier because of its high octanol/water coefficient, we speculate that part of the metallic mercury deposited in the subcutaneous and muscular tissues, during the beginning of the follow-up, was slowly but regularly released into the bloodstream as Hg<sup>2+</sup> resulting in a greater urinary excretion, and a lesser passage through blood-brain barrier.<sup>1</sup> The steep decrease in urinary Hg, despite the definite presence of Hg tissue deposits, in the second part of the follow-up, probably reflects changes in the biological bioavailability of metallic Hg from surface deposits, secondary to fibrotic scarring around them, or possible transformation of Hg<sup>2+</sup> into less absorbed chemical species. *Reference:* 1. Romero IA, Abbott NJ, Bradbury MWB. The blood-brain barrier in normal CNS and in metal-induced neurotoxicity. In: Chang LW, ed. Toxicology of Metals. Boca Raton, US: CRC Press, 1996:561–85.

### 177. Caffeine Poisoning Causing Prolonged Lactic Acidosis, Hyperglycemia, Hypokalemia and Leukocytosis

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*Objective:* Severe caffeine overdoses may be associated with metabolic disturbances leading to a complex and

possibly misleading clinical picture. *Case report:* A 29-year-old man being treated with methylphenidate ingested 210 caffeine tablets of 100 mg each (21 g) in a suicide attempt. On arrival at hospital three hours later he was awake and presented gastrointestinal symptoms including repeated vomiting. ECG displayed sinus tachycardia, 110 b/m. Arterial blood-gas analyses showed pH 7.2, base excess -15 mmol/L and serum lactate 10 mmol/L. A hypokalemia of 2.1 mmol/L was evident and the white cell blood count was elevated to 23 x 10<sup>9</sup>/L. A blood glucose of 18 mmol/L and ketones present in the urine initially raised suspicion of a previously unrecognized diabetic disorder with ketoacidosis. The patient was given fluids, small volumes of buffer solution, insulin and potassium intravenously. Despite these measures, the serum lactate remained at the same high level for almost ten hours before it gradually normalized. Other causes of lactic acidosis, such as seizures or circulatory failure, never occurred. No signs of diabetes mellitus remained afterwards and the patient was discharged early at day three after the suicide attempt. *Discussion:* A search in PubMed yielded two previous case reports of caffeine induced lactic acidosis.<sup>1,2</sup> Caffeine gives rise to excessive sympathetic stimulation with increased glycogenolysis and lipolysis resulting in hyperglycemia. Subsequently a secondary rise in pyruvate occurs. Pyruvate can be further converted to lactate if the aerobic pathway is insufficient. Caffeine induced sympathetic alpha-adrenergic vasoconstriction may create anaerobic conditions locally in the tissues, thus promoting lactate formation. Elevated levels of catecholamines also shift potassium into the intracellular compartment through a beta2-adrenergic response and a blockade of adenosine receptors. *Conclusion:* A toxidrome consisting of hyperglycemia, hypokalemia, leukocytosis and lactic acidosis may be seen after intake of caffeine in high doses. *References:* 1. Schmidt A, Karlson-Stiber C. Caffeine poisoning and lactate rise: an overlooked toxic effect? Acta Anaesthesiol Scand 2008; 52:1012–4. 2. de Wijckerslooth LRH, Koch BC, Malingré MM, et al. Life-threatening hypokalaemia and lactate accumulation after auto-intoxication with Stacker 2, a ‘powerful slimming agent’. Br J Clin Pharmacol 2008; 66:728–31.

### 178. Forgotten but not Gone – A Case of Cardiac Dysrhythmia Following Phenylpropanolamine Ingestion

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*Objective:* Phenylpropanolamine (PPA) is an alpha-adrenergic agonist that was once marketed in the USA both as a decongestant and appetite suppressant. A study completed in 2000 linked it to an increased risk of hemorrhagic stroke in women, and although never officially withdrawn from the market, a request to manufacturers from the FDA for voluntary withdrawal from products greatly reduced its availability. Despite this a large number of households still retain medicinal products containing PPA in old or expired medications. In fact, there were over 3000 exposures reported to US Poison Centers for PPA in 2009. While overdose of PPA is well known to cause increased blood pressure with a resultant bradycardia, other types of atrial and ventricular dysrhythmia have been reported. We present a case of torsade de pointes (TdP) in a patient who overdosed on a PPA product that she had been hoarding since

1989. *Case report:* A 55 year-old woman presented to the Emergency Department after ingesting 30 tablets of an expired cough and cold medication from 1989 that contained guaifenesin and phenylpropranolamine in addition to 15 pregabalin 25 mg tablets. Shortly after ingestion the patient developed persistently elevated blood pressure (140–150's systolic/90–110's diastolic (mean arterial pressure 105–110 mmHg) and sinus bradycardia (40 bpm) as well as a frontal headache. In the 20 hours following her presentation, the patient had two episodes of syncope. The first episode was not recorded but during the second episode, recorded as the patient had gotten out of bed to walk to the bathroom, a period of polymorphic wide-complex tachycardia coincided with the loss of consciousness. As this occurred the heart rate transiently increased to 90 beats-minute and the QT interval, measured on the telemetry tracing, increased to 520 msec (QTc 637). Atrial and ventricular ectopy were also evident on telemetry prior to the arrhythmia. *Conclusion:* TdP has been documented in animal PPA ingestions. To our knowledge, this is the first reported case of TdP with PPA overdose in humans. Neither of the patient's coingestants – pregabalin and guaifenesin – has ever been associated with a ventricular dysrhythmia.

#### 179. Seizures in the Setting of Large Pregabalin Overdose

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*Objective:* Pregabalin is a medication used most often for adjunctive treatment of seizure disorders and neuropathic pain. As a GABA analogue, it works at the GABA receptor in the CNS, although the exact mechanism of action is not well understood. Significant overdose of pregabalin usually results in CNS depression, ranging from drowsiness to coma. Although uncommon, some anti-seizure medications are known to cause seizures in overdose (e.g. phenytoin, lamotrigine, carbamazepine). However, neither pregabalin nor its close relative gabapentin have previously been associated with this effect. Seizures were reported in one patient who ingested pregabalin with lamotrigine, but the seizures in this case can reasonably be attributed to lamotrigine. *Case report:* A 54 year old female presented to the Emergency Department after ingesting 51 tablets of pregabalin 75 mg (3825 mg). Her history was significant for cocaine, opioid, and ethanol abuse, although she denied current use of these chemicals. Although awake and alert upon presentation, she quickly deteriorated to a state of obtundation responding only to deep sternal rub. Despite this she was maintaining her airway and did not require intubation. At approximately 10 hours post ingestion, the patient had a witnessed tonic-clonic seizure with right gaze deviation, foaming at the mouth, and involuntary mouth movements. The seizure was self-limited, lasting approximately one minute. Upon resolution the patient returned to an obtunded state. She was given a single dose of 1 mg lorazepam IV immediately following the seizure. She continued to be managed with supportive care, and over the next few hours she returned to baseline mental state. A pregabalin level drawn approximately five hours post ingestion was 58 micrograms/mL (chronic daily doses of 150 and 600 mg/day result in steady-state levels averaging 1.3 mg/L and 4.9 mg/L respectively<sup>1</sup>). *Conclusion:* To our knowledge, this is the first case of a seizure associated with isolated pregabalin overdose. The serum level observed in this patient is among the highest reported in the litera-

ture. The potential mechanism of a pregabalin-induced seizure is unknown. *Reference:* 1. Baselt RC. Disposition of Toxic Drugs and Chemicals in Man. 8th ed. Foster City, US: Biomedical Publications, 2008.

#### 180. Are Ingested Lithium Tablets Visible on X-ray? A One Year Prospective Survey

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*Objective:* The radiopacity of lithium tablets is not fully determined. We found only two reports investigating this question, both *in vitro* studies. One found two lithium preparations to be moderately detectable by plain radiography.<sup>1</sup> The other study, using computed tomography (CT), found one preparation of lithium carbonate to be weakly-moderately detectable, while a lithium carbonate preparation from another manufacturer was not detectable at all.<sup>2</sup> *Methods:* We performed a prospective survey during the year 2010 of our inquiries to the poison centre concerning lithium poisoning. All patients who presented with a suspected intake of more than 19 lithium tablets within six hours before the call were included and followed up. If advisable, we recommended the performance of an acute abdominal x-ray. The only lithium tablet approved in Sweden, is a slow-release preparation containing 42 mg of lithium sulphate. *Results:* A total of 14 cases were included. In two patients no x-ray was performed. In six patients plain radiography was performed, all with a negative result. The remaining six patients were examined by abdominal CT. In five of these latter patients, tablets were clearly visible in the GI-tract. All 14 patients developed toxic serum lithium concentrations. Two cases are summarized as follows: 1. A 56-year-old man ingested 70 lithium tablets. A CT scan approximately two hours after ingestion showed numerous tablets in the ventricle and duodenum. Gastric lavage was performed and whole bowel irrigation was started 3.5 hours after intake. The serum lithium concentration reached a maximum of 5.0 mmol/L. The patient received treatment with hemodialysis. 2. A 46-year-old man presented to hospital 5–6 hours after a suspected intake of 84 lithium and 30–40 zopiclone tablets. A CT scan revealed several tablets clearly visible in the GI-tract. Gastric lavage resulted in the retrieval of tablets. The serum lithium increased to a maximum of 1.7 mmol/L. *Conclusion:* Based on these findings, ingested slow-release lithium sulphate tablets may be visible on abdominal CT. The use of plain radiography seems less appropriate. *References:* 1. O'Brien RP, McGeehan PA, Helmezi AW, et al. Detectability of drug tablets and capsules by plain radiography. *Am J Emerg Med* 1986; 4:302–12. 2. Savitt DL, Hawkins HH, Roberts JR. The radiopacity of ingested medications. *Ann Emerg Med* 1987; 16:331–9.

#### 181. Toxicity Profile of Methocarbamol: A Retrospective Study from the French Poison and Toxicovigilance Centres

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*Objective:* Following one case of severe poisoning involving methocarbamol, the French Health Product Safety Agency (Afssaps) requested the National Coordination Committee for Toxicovigilance to assess the methocarbamol toxicity profile. Methocarbamol is a muscle relaxant with a carbamate function which is chemically close to meprobamate whose severe toxicity is well known. *Methods:* All cases of exposure to methocarbamol reported to the French poison and toxicovigilance centres from January 1, 2000 to November 15, 2010 were analyzed. Associations with other drugs, circumstances of exposure, age, estimated dose and symptoms were recorded. Coma (Glasgow score under 8), hypotension (systemic arterial pressure under 80 mmHg), cardiovascular shock, hypothermia (body temperature under 35°C), bradypnea, apnea, cyanosis or death were noted as severity criteria. *Results:* 473 cases were collected in which 258 showed symptoms (47 involving only methocarbamol, 211 concerning poly-intoxicated patients). The main circumstance of exposure was suicide attempt (345 out of 473 cases). Estimated ingested doses (EID) ranged from 0.25 to 45 g (0.5 to 20 g in asymptomatic cases). Among the 47 symptomatic cases with only methocarbamol exposure, EID varied from 0.5 to 30 g; 32 cases concerned suicide attempts; drowsiness was the most frequent reported symptom; no serious case was described in this group. Among the 211 symptomatic cases involving several medications, 184 were suicide attempts with methocarbamol; EID ranging from 0.5 to 45 g. Twelve serious poisoning cases were described; in most cases, symptoms could be related to other co-ingested medications but in 3 cases methocarbamol was suspected to contribute to hypotension, vasoplegia, drowsiness or cardiac arrest. Of the 3 deaths reported, methocarbamol responsibility was not likely because of its plasma concentration at therapeutic level or presence of meprobamate or dextropropoxyphene in very toxic concentrations. *Conclusion:* Four cases of deaths involving methocarbamol were published previously. Afssaps was concerned about severe poisonings of this muscle relaxant, taking also into account the chemical relationship with meprobamate. The data obtained in this reassuring retrospective study do not support a future modification of the SPC nor the setting up of a risk reduction procedure as was recently done with meprobamate in France.

#### 182. Comparative Toxicity of Benzodiazepine and Non-Benzodiazepine Sedative-Hypnotics Following Intentional Drug Overdose

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*Objective:* The prevalence of sedative-hypnotic abuse is increasing in Taiwan. Intentional overdose of sedative-hypnotics can lead to various toxic effects such as drowsiness, hypotension, respiratory depression and coma. However, very few studies had been conducted to evaluate the comparative toxicity of different sedative-hypnotics following intentional drug overdose. *Methods:* We analyzed all patients with intentional sedative-hypnotic overdose admitted to a tertiary medical center in Taiwan between 2004 and 2008. After excluding patients with accidental sedative-hypnotics overdose and patients with concomitant exposure to highly toxic substances (e.g. organophosphates and paraquat), we reviewed and abstracted the medical records of all eligible patients. Descriptive statistics and multivariate logistic regression analysis were then employed to analyze the data. *Results:* A total of 533

cases were eligible for final analysis. Most cases were females (63.6%), aged between 20 and 49 years old (65.5%), were exposed to benzodiazepines ( $n = 361$ ), and attempted suicide (89.9%). Among them, coma and other depressant effects of the central nervous system were the most common manifestations; and 216 patients (40.5%) received flumazenil therapy. Sixty-seven patients (12.6%) required admission to intensive care unit and 6 patients (1.1%) died. In multivariate analyses, a Glasgow Coma Score  $\leq 7$  (OR 16.1, 95% CI 4.5–7.9) and the presence of aspiration pneumonia (OR 3.6, 95% CI 1.6–57.9) were more likely to be associated with severe/fatal effects; whereas non-benzodiazepines (including zolpidem and zopiclone) were associated with a lower toxicity (OR 0.4, 95% CI 0.2–0.9). **Conclusion:** Benzodiazepine sedative-hypnotics, severe coma, and aspiration pneumonia were associated with more severe effects following intentional sedative-hypnotics overdose in Taiwan.

### 183. Takotsubo Cardiomyopathy Associated with Sudden Benzodiazepine Withdrawal

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**Objective:** We report a case of Takotsubo cardiomyopathy (transient left ventricular apical ballooning syndrome) associated with sudden benzodiazepine withdrawal. **Case report:** A 49-year-old woman with a history of diabetes mellitus, borderline personality disorder, benzodiazepine dependence and convulsions took 300 mg of zolpidem. On admission to hospital 2 hours later, she was alert and physical examination and ECG were normal. Activated charcoal was administered. Her usual medications (gliclazide MR, metoprolol, chlorpromazine, fluoxetine, lorazepam 2 mg nocte and zolpidem 50 mg nocte) were temporarily withdrawn after hospital admission. She remained stable until 28 hours post-ingestion when she suddenly developed a brief episode of generalised tonic-clonic convulsion. Physical examination showed bilateral hand tremors which were compatible with benzodiazepine withdrawal. ECG showed ST segment elevation in lead II and supraventricular tachycardia (HR 154 bpm) which was terminated by an intravenous injection of adenosine 10 mg. Plasma electrolytes and glucose, CAT scan of brain and EEG were normal. Arterial blood gas analyses showed mild metabolic acidosis with respiratory compensation. Urine drug screen by LCMS revealed her usual medications only. However, serial ECGs and cardiac enzymes were abnormal (persistent ST elevation over leads V2 to V6, II, III, and aVF; CPK 4231 U/L, plasma troponin T 0.69 microgram/L). She was treated with subcutaneous enoxaparin and aspirin. Echocardiogram showed apical akinesia with left ventricular ejection fraction of 45%. Coronary angiogram showed normal coronary vessels, but a mild systolic bridging was noted over the distal left anterior descending coronary artery. Echocardiograms at 4 days and 7 weeks showed a normal apical wall movement but an abnormal left ventricular relaxation pattern during the diastole. **Conclusion:** The clinical features in this patient were compatible with a diagnosis of Takotsubo cardiomyopathy based on the criteria proposed by Prasad.<sup>1</sup> In two-thirds of patients, sudden precipitating events (emotional or physical stress) with catecholamine excess can be identified. Alcohol withdrawal as a triggering factor had previously been reported.<sup>2</sup> Similarly, benzodiazepine withdrawal can induce catecholamine surge.<sup>3</sup> Patients with Takotsubo cardiomyopathy usu-

ally recover after conservative management. Sudden benzodiazepine withdrawal in a patient with benzodiazepine dependence should be avoided as this may result in convulsions, acute withdrawal symptoms and Takotsubo cardiomyopathy. **References:** 1. Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. *Am Heart J* 2008; 155:408–17. 2. Joakim A, Leila B, Laure CR, et al. Takotsubo cardiomyopathy triggered by alcohol withdrawal. *Drug Alcohol Rev* 2011; 30:434–7. 3. Duka T, Ackenheil M, Noderer J, et al. Changes in noradrenaline plasma levels and behavioural responses induced by benzodiazepine agonists with the benzodiazepine antagonist Ro 15–1788. *Psychopharmacology (Berl)* 1986; 90:351–7.

### 184. Successful Treatment of Serotonin Syndrome with Sublingual Olanzapine

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**Objective:** Serotonin syndrome is a potentially life-threatening condition, caused by an overstimulation of the postsynaptic 5-HT<sub>1A</sub> and 5-HT<sub>2</sub> receptors owing to increased serotonin levels in the synapses. Such an increase can be induced by an overdose of drugs that e.g. inhibit the presynaptic reuptake of serotonin or inhibit its enzymatic inactivation. The clinical manifestations of the serotonin syndrome are a triad of symptoms including altered mental status, autonomic dysfunction and neuromuscular abnormalities. Cyproheptadine is the most commonly used treatment for serotonin syndrome, but it has the disadvantage that it only can be administered orally. Olanzapine, an atypical antipsychotic drug with both serotonin and dopamine antagonistic effects, has in one earlier study shown good results when administered to patients with serotonin syndrome.<sup>1</sup> We report a case of a patient with serotonin syndrome treated with olanzapine. **Case report:** A 46-year-old woman with a history of depression and alcohol overconsumption presented to hospital after ingestion of 3 g venlafaxine and alcohol. On admission she had CNS-depression, tachycardia (150 beats/minute), signs of dehydration and a short seizure episode. She was treated with IV fluids, diazepam and metoprolol. Soon after admission the patient developed hyperthermia and during the following hours her condition deteriorated with increasing hyperthermia (39–40 °C), confusion, restlessness, hyperreflexia, myoclonia, seizures and increased creatine-kinase, all indicating serotonin syndrome. Olanzapine 5 mg was administered sublingually and the patient's condition improved dramatically. Immediately her pulse fell to 100 beats/minute and she became calm. Within a couple of hours her temperature was normalised. **Conclusion:** This case confirms that olanzapine is an effective treatment for serotonin syndrome. The sublingual absorption of olanzapine is rapid and this is reflected by an immediate treatment effect. **Reference:** 1. Boddy R, Dowsett RP, Jeganathan D. Sublingual olanzapine for the treatment of serotonin syndrome. *Clinical Toxicology* 2006; 44:439–40.

### 185. Atomoxetine – Accidental Ingestion Seems Rarely Dangerous

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**Objective:** There are a limited number of reports with regard to atomoxetine overdose. The dose-response relationship is unclear. To get more information we analysed poisons centre data in the Society of Clinical Toxicology of German Speaking Countries (GfKT). **Methods:** Multi-centric retrospective analysis of cases reported to poisons centres in Germany. The centres were asked to send cases meeting the following criteria: 1: Mono-intoxication 2: Uncertainty in the dose less than 10 percent. 3: Follow up for at least 6 hours. The centres were encouraged to send additional cases not meeting these criteria if they consider them to be useful to describe special aspects of atomoxetine toxicity. **Results:** 51 submitted cases met the criteria. Fifteen additional cases were considered because of the symptoms developed. Eleven patients were younger than 6 years, 24 patients 6 to 13 years old, 31 patients were 14 years and older. Most common symptoms were drowsiness (19 patients), mydriasis (11 patients), nausea or emesis (10 patients), tachycardia (9 patients), restlessness or mild agitation (5 patients). More severe symptoms were seizures, stupor, coma (one with, one without respiratory depression), hallucinations, more pronounced agitation or tachycardia. Severity of symptoms was graded according to the poisoning severity score. Mean atomoxetine dose was 3.9 mg/kg (0.54 to 32.3) in asymptomatic patients and 6.8 mg/kg (0.62 to 55.6 mg/kg) in patients with mild symptoms. Moderate symptoms resulted from ingesting 5.6 mg/kg, 15 mg/kg, or snuffing up to 12.4 mg/kg atomoxetine respectively. Severe symptoms were caused by 37.3 mg/kg and by 80 tablets of unknown atomoxetine content. In patients without prior treatment with atomoxetine and mild symptoms the mean dose was 8.3 mg/kg whereas in patients who regularly took atomoxetine this dose was 2.8 mg/kg. **Conclusion:** The individual tolerance to atomoxetine overdose is very variable. Severe symptoms like coma, seizures or severe agitation can occur in high doses. Ingestion of up to 2 or 3 times the maximum daily dose (related to body weight) usually results in mild symptoms. Pretreated patients may be more prone to develop symptoms than patients naïve to atomoxetine.

### 186. Severe Intentional Pentobarbital Poisoning

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**Objectives:** This case report is a presentation of a rare case of severe intentional pentobarbital poisoning. Pentobarbital is a quickly absorbable, shorter-acting barbiturate. **Case report:** A 48-year-old male attempted suicide by consuming porridge sprinkled with a handful of pentobarbital. The pentobarbital was pure raw material for drug manufacturing purposes. The patient was currently healthy, with a history of hypertension and mild depression, but active and working in the pharmaceutical industry. Fifteen minutes after the ingestion he became increasingly disorientated and unconscious. On arrival of medical assistance the patient had impaired respiration, GCS 3 and was cyanotic. Immediate intubation at home was necessary. Subsequent intensive care unit admission data were: BP 96/67 mmHg (mean arterial pressure 77 mmHg), HR 95 min<sup>-1</sup>, T(rectal)

35.4 C, miotic pupils reacting to light, serum-ethanol 63 mmol/L, lactate 2.2 mmol/L. The ECG showed sinus rhythm and normal ST-segment. Two hours after the drug ingestion gastric lavage was performed followed by instillation of activated charcoal (50 g at two hours and six hours). Urine-quicktests showed positive drug-screen for barbiturate only. The following days the patient stayed comatose, in a hypertensive state (BP 215/96 mmHg (mean arterial pressure 136 mmHg), HR 97 min<sup>-1</sup>), T(rectal) 39.0 C, pupils were miotic. Two seizure episodes were effectively treated (IV clonazepam 0.5 mg). CT-cerebrum, arterial blood gas, and x-ray (thorax) were all normal. Aspiration pneumonia was suspected (elevated CRP and Haemophilus influenzae findings in tracheal secrete) and antibiotics (cefuroxime 1500 mg x3/day, metronidazole 500 mg x3/day) were initiated. Labetalol 10 mg p.n. and clonidine 50 microgram x3/day were initiated to treat the hypertension. Intravenous propofol (120 mg/h) was administered from day-3, as concomitant intake of sympathomimetics was suspected due to continued hypertension and hyperthermia. All parameters normalised on day-4, and the patient was extubated. He admitted ingesting significant amounts of pentobarbital concomitant with alcohol, and explained that he used pentobarbital at home for ant control. **Conclusion:** Severe pentobarbital poisoning is infrequent as access to the drug is rarely possible for non-professionals. Pentobarbital is approved in Denmark for euthanasia of animals only. Serum-pentobarbital concentration determination was unfortunately unavailable. The hypertension observed day 2-5 was possibly an untreated pre-existing condition, but the seizures could not be explained from the pentobarbital ingestion. Anamnesis and the fast onset of severe systemic toxic reactions supported the significant pentobarbital ingestion.

#### 187. Cholinergic and Adenosine Receptor Stimulation in Cognitive Improvement after Anticholinergic Toxicity

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**Objective:** Acute poisonings by medications with central anticholinergic action cause memory impairment, increase anxiety, and decrease patient's social activity. Choline alfoscerate (acetylcholine precursor) (CAS) and Cytoflavin (a Russian pharmaceutical consisting of nicotinamide, inosine, riboflavin, sodium succinate and glucamine) (CYT) have been associated with neuroprotective effects and may ameliorate anticholinergic toxicity after acute poisonings by anticholinergic agents. **Methods:** Seventeen randomly distributed patients (16-38 y.o., 10 m, 7 f) admitted to the rural hospitals of Leningrad Region with acute poisoning by neuroleptics, tricyclic antidepressants, antihistamines of moderate severity (3+)<sup>1</sup>. Interventions were identical (decontamination, forced diuresis, administration of antidotes) except that the "treated" group (n = 10) received CAS (1 g, IV, b.i.d.) and CYT (10 cc in 5% dextrose solution b.i.d.) from the 1st day of admission until anticholinergic hyperactivity was over. Observations were made after 48 h of stay in the hospital and on 10th day by active telephone calls to patients. Measurements included physical examination for specific signs, Glasgow Coma Score (GCS), ECG-test, complete blood count, urinalysis, thin layer chromatography. Memory, cognitive functions, and social adaptation were recorded by question-

naires (10 word-test), Mini Mental Scale Examination (MMSE), and Bartel Scale, respectively. Statistics were done using Wilcoxon "U" criteria. **Results:** On admission GCS = 10.1 ± 0.5 (controls), 9.8 ± 1 (treated), p > 0.05. After 48 h: GCS = 12.4 ± 0.3 (controls), 13.8 ± 0.5 (treated), p ≥ 0.05; MMSE = 13.14 ± 1.5 (controls), 18.5 ± 1.06 (treated), p < 0.05. Short-term memory 3.3 ± 0.3 (controls), 4.7 ± 0.5 (treated), p = 0.05. After 10 days, in controls cognitive and short-term memory functions were decreased to 22% and 12%, correspondingly, in comparison to the treated group, p < 0.05; long-term memory was decreased to 32%. **Conclusions:** Choline alfoscerate and Cytoflavin increase memory and cognitive functions after acute poisonings by anticholinergic medications. **Reference:** 1. Pousada L, Osborn HH, Levy DB. Emergency Medicine for the House Officer, 2nd ed. Baltimore, US: Williams and Wilkins, 1996: 183.

#### 188. First Reported Case of Acute Prolonged Neuropsychiatric Toxicity Associated With Analytically Confirmed Recreational Use of Phenazepam

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**Objective:** There has been increasing availability and recreational use of benzodiazepines purchased from Internet 'legal high' and 'research chemical' suppliers over recent years. Benzodiazepines available include both those that are widely used and licensed for pharmaceutical use across Europe (e.g. diazepam and temazepam) and also those that are not used in Europe (e.g. phenazepam and etizolam). The UK government placed an import ban on phenazepam (sometimes termed fenazepam) in July 2011 to try and decrease its availability. We report here the first case of analytically confirmed acute phenazepam toxicity. **Case report:** A 42 year old male with no previous medical or psychiatric history was brought to the Emergency Department by his friends because he had been found confused and disorientated approximately 24 hours after nasal insufflation of up to 1g of three "white powders" that he had purchased from the Internet. The white powders were in individual zip-locked bags and labelled as "not for human consumption", "plant food" and "research chemicals", the patient and his friends did not know what the drugs were. On arrival in the Emergency Department he was confused and disorientated in time, place and person. His pupils were dilated (5 mm) but he had a normal temperature (35.8°C), heart rate (72 bpm) and blood pressure (119/80 mmHg) and neurological examination was normal. He was admitted for observation, and his neuropsychiatric symptoms of confusion and disorientation settled gradually over the next 48 hours. He was then discharged home with no sequelae. **Toxicological Screening:** A serum sample was collected and analysed by gas chromatography-mass spectrometry (GC-MS). The only drug found on a comprehensive toxicological screen was phenazepam at a concentration of 0.49 mg/L (therapeutic concentration < 0.03 mg/L). **Conclusion:** We report here a patient with prolonged neuropsychiatric symptoms of confusion and disorientation lasting for 72 hours after use of phenazepam bought from an Internet 'legal high' supplier. Clinical toxicologists and emergency physicians should consider phenazepam and other long acting benzodiazepine toxicity in patients

presenting with prolonged neuropsychiatric features after recreational drug use.

#### 189. Overdose of Selective Serotonin (5HT1) Agonists

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**Objective:** The aim of the study was to assess the toxicity of serotonin (5HT1) agonists in overdose, because there is little information in the literature on this topic. **Methods:** In a retrospective study, cases of overdose of serotonin (5HT1) agonists from nine Poisons Information Centres in Austria, Germany, and Switzerland were analysed. Inclusion criteria were mono-intoxication, defined dose, and documented follow up. **Results:** In total, 59 cases of poisoning by serotonin (5HT1) agonists were registered (almotriptan 3, eletriptan 3, frovatriptan 3, naratriptan 13, rizatriptan 7, sumatriptan 10, zolmitriptan 20). Patients involved were 42 children (0.08-13 years) and 17 adolescents and adults (17-57 years). Doses expressed as a multiple of the maximum single dose for adults ranged between 0.125-2 (median 1) in children and 1-50 (median 4) in adolescents/adults. Sixty-seven per cent of children remained asymptomatic, 31% developed mild symptoms. Only a one-month-old baby suffered from moderate symptoms with dyspnoea and respiratory acidosis after nasal application of 5 mg zolmitriptan. In adolescents/adults almost half of the patients developed mild (35.3%) or moderate symptoms (11.8%). Most frequent symptoms were fatigue (23%), somnolence (18%), hypertension (18%), nausea/vomiting (18%), dizziness (14%), and tachycardia (9%). In moderate poisonings, pronounced hypertension and angina pectoris were observed in an adult and an adolescent after ingestion of a 4-fold and 6-fold maximum single dose of sumatriptan and naratriptan, respectively. **Conclusion:** After ingestion of a dose up to the maximum single dose for adults by children, there was no or only mild toxicity. This is in accordance with the results of previous studies suggesting observation at home for children with unintentional ingestion of an adult therapeutic dose.<sup>1,2</sup> In adults, doses from the 4-6-fold maximum single dose can induce moderate toxicity. However, the final assessment of toxicity of serotonin (5HT1) agonists requires further studies with more cases. **References:** 1. Borys D, Hill K, Morgan D. Triptans in pediatric overdose. Is medical treatment necessary? Clin Toxicol 2002; 40:665-6. 2. Des Lauriers C, Burda A. Pediatric ingestions of triptans. Clin Toxicol 2008; 46:614.

#### 190. A Case of Extraordinary High Serum-Venlafaxine and Prolonged Elimination without Genetic Predisposal

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**Objective:** Venlafaxine is a bicyclic antidepressant not structurally related to any conventional anti-depressant medications. It has two metabolites, of which one is active (O-desmethyl venlafaxine) and one is inactive (N-desmethyl venlafaxine). Both the parent drug and the active metabolite inhibit monoamine uptake (serotonin > noradrenaline >> dopamine). We present a poisoning with a very high concentration of S-venlafaxine with a prolonged course, different complications and a favorable outcome. Kinetics and genetic variations are discussed. **Methods:** A 44-year-old male was found after a suicidal attempt with 15 g of venlafaxine (extended release preparation) and 1.5 g of chlorprothixen. He was initially unconscious; he had seizures, and an observed pulseless VT. Cardiopulmonary resuscitation and gastric lavage were performed, and charcoal instilled. His initial S-venlafaxine was 19,400, S-O-demethyl venlafaxine 15,100. Creatine kinase (CK) was approx. 60,000, and myoglobin twelve hours after admission was 24,000. He had a prolonged course with an acute renal failure (dialysis for 10 days) and need for mechanical ventilation for 5 days. His S-half-lives were: S-venlafaxine 15.4 hours (n = 11, OT = 163 hours, R<sup>2</sup> = 0.97) and serum-O-demethyl venlafaxine 31.9 hours (n = 11, OT = 163 hours, R<sup>2</sup> = 0.93). A therapeutic level of chlorprothixen was also found in serum. He was screened for 74 additional substances; all found negative. A pharmacogenetic analysis was also performed for the CYP2C9, CYP2C19, and CYP2D6, all found without mutations. **Conclusion:** The present case illustrates the typical course of a severe venlafaxine overdose, with unconsciousness, seizures, rhabdomyolysis, and ECG changes. He did, however, have an unusually high serum concentration, a prolonged elimination period, and a surprisingly high myoglobin as compared to his CK. The outcome of his renal function was favorable.

### 191. Findings of Delayed Nicotinic Toxicity in Varenicline Overdose

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**Objective:** Varenicline is an alpha4beta2 neuronal nicotinic receptor partial agonist recently introduced as a smoking cessation aid. Its properties in human overdose are poorly understood because of few case reports. The limited data available do not demonstrate loss of receptor specificity in overdose and instead describe vomiting, tachycardia and neuropsychiatric abnormalities.<sup>1-3</sup> We describe a patient with intentional varenicline ingestion who presented with vomiting, diarrhea, depressed level of alertness and bradycardia consistent with delayed nicotine toxicity. **Case report:** A 39 year-old woman with past medical history significant for depression arrived by ambulance after she was found vomiting and having diarrhea following an intentional overdose approximately 3 hours prior to presentation. Emergency medical services reported finding a varenicline starter pack with eleven 0.5 mg and fourteen 1 mg (total 19.5 mg) missing. On physical exam she was drowsy but rousable to physical stimulation. Heart rate ranged from 34 to 46, blood pressure was 94/47 mmHg, rectal temperature was 95.6F (35.3C), and oxygen saturation was 100% on 2 liters nasal cannula. She was retching and incontinent of stool. Her pupils were 3 mm and reactive. Bowel sounds were hyperactive. The remainder of the exam was unremarkable. She was intubated for airway protection. She recovered fully in 72 hours with supportive

care. On recovery, she admitted to taking 3 alprazolam unknown strength tablets, 3 acetaminophen unknown strength tablets, an unknown amount of venlafaxine, and all of her varenicline tablets. **Conclusion:** We present the first report of classic findings of delayed nicotine poisoning following intentional overdose of varenicline. This suggests varenicline loses its alpha4beta2 neuronal nicotinic receptor specificity in overdose. **References:** 1. Feng S, Goto CS, Velez LI, et al. Varenicline (Chantix registered) overdose in an adolescent female. *Clin Toxicol* 2008; 46:362. 2. Kreshak AA, Clark AK, Clark RF, et al. A retrospective poison center review of varenicline-exposed patients. *Ann Pharmacother* 2009; 43:1986-91. 3. Rollema H, Faessel HM, Williams, KE. Varenicline overdose in a teenager - a clinical pharmacology perspective. *Clin Toxicol (Phila)* 2009; 47:605.

### 192. Life Threatening Cardiac Arrhythmias in Massive Acute Valproic Acid Overdose

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**Objective:** Valproic acid (VPA) is a broad-spectrum antiepileptic drug that is now used commonly for several other neurological and psychiatric indications. Although VPA is known for its quinidine-like effects on cardiac conduction and has been described as stimulating potassium urinary excretion in experimental animals, life threatening cardiac arrhythmias following acute VPA overdose have been rarely reported. **Case report:** A 72-year old man being treated with VPA for a psychiatric disorder was admitted to our emergency department with a reported self ingestion of 60 g prolonged release sodium valproate. On examination, he was miotic, apyretic and looked clinically dehydrated. His heart rate was 70 bpm, rhythmic, blood pressure 130/75 mm Hg. He showed a decreased response of deep tendon reflexes and was conscious with Glasgow coma score (GCS) 15. The total VPA plasma concentration was 2239 mg/L associated with hyperammonemia (310 micrograms/dL), hypokalemia (2.7 mEq/L) and ECG QTc prolongation (528 msec). We immediately performed gastric lavage, administered multiple doses of activated charcoal and started hydration. The patient's conscious level worsened in two hours (GCS 6) and it became necessary to proceed with oro-tracheal intubation and ventilation. At the same time, he suffered ventricular tachycardia runs unresponsive to antiarrhythmic drugs and junctional rhythm with hemodynamic instability contraindicating the hemodialysis/hemoperfusion enhanced elimination of the drug. A temporary intracavitary cardiac pacing was placed and removed on the fourth day with a complete recovery of cardiac function and a concomitant return of serum valproic acid therapeutic concentration and normalization of serum potassium level. Twelve hours after arrival we started levocarnitine administration in order to reduce hyperammonemia which normalized within 24 h. In day 4-6 the patient experienced transient thrombocytopenia (16,000) which required repeated platelet transfusion. The patient remained in hospital for 13 days due to lung comorbidity and was discharged in good health condition. **Conclusion:** Massive acute VPA intoxication can be complicated by complex, rarely reported and life threatening cardiac arrhythmias probably sustained by valproic acid induced quinidine-like effect and hypokalemia. Moreover, valproic acid induced hyper-

ammonemia and thrombocytopenia must be carefully evaluated.<sup>1</sup> **Reference:** 1. Sztajnkrzyer MD. Valproic Acid Toxicity: Overview and Management. *J Toxicol Clin Toxicol* 2002; 40:789-801.

### 193. Bradycardia in a Carbamazepine Overdose: A Case Report

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**Objective:** Carbamazepine (CBZ) is an antiepileptic drug used in epilepsy and also in the treatment of neuropathic pain and bipolar disorder. CBZ has quinidine-like effects on cardiac conduction. Bradyarrhythmias or atrioventricular conduction delays have rarely been reported, predominantly in elderly women during chronic therapy.<sup>1</sup> **Case report:** We describe the case of a 66-year old woman admitted to our Toxicology Unit for a self-induced overdose with CBZ. The patient had taken 12 g of extended-release tablets from her husband 3 hours before reaching the hospital. On arrival she presented alert and cooperative, vital parameters were in range. She received oral administration of 50 g of activated charcoal in order to reduce drug absorption. Fluid IV therapy with saline solutions and sodium bicarbonate 1.4% were started and continued for 5 days. A 12-lead ECG showed regular sinus rhythm. Serum CBZ levels were continuously monitored throughout hospitalization. At the 6th hour post-ingestion, vomiting associated with disorientation, facial trismus, upward eye movement and conspicuous mydriasis occurred. Her heart rate dropped to 38 b/m, urging the IV administration of a bolus of 1 mEq/kg body weight sodium bicarbonate and 1 mg atropine which reverted bradycardia in a few minutes. A similar pattern flared after three hours and a third one occurred at the 16th hour post-ingestion. By that time the ECG showed a junctional rhythm with 38 to 42 b/m which tended to recur during the next 24-hour period and was monitored for 72 hours. The time course of serum CBZ levels was strictly related to the heart rate decrease. During the following days a continuous 24h-ECG was performed, showing normal rhythm. The patient was transferred to the psychiatric ward on 7th post-ingestion day. **Conclusion:** The present case shows how ECG monitoring is required especially in elderly women in CBZ overdose, as potentially life-threatening bradyarrhythmias or atrioventricular conduction delays may occur either with therapeutic or elevated CBZ serum levels. **Reference:** 1. Kasarskis EJ, Kuo CS, Berger R, et al. Carbamazepine-induced cardiac dysfunction. *Arch Intern Med* 1992; 152:186-91.

### 194. Toxicity of Mirtazapine Overdose: Results of a Multicentre Retrospective Review

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**Objective:** The toxicity of mirtazapine overdose is considered to be low. However, the number of mono-intoxications published so far is limited, especially in children and elderly people. We therefore investigated overdoses of mirtazapine in a larger number of patients. **Methods:** In a multicenter retrospective study, cases of mirtazapine overdose reported to German, Austrian, and Swiss Poisons Information Centres were analysed. Important inclusion criteria were monointoxication with mirtazapine, defined dose and follow-up for at least four hours after ingestion. **Results:** A total of 493 cases were analysed. In 50 toddlers (age 1–< 6 years) the ingested dose ranged from 15 to 180 mg. In 17 children ingesting 15 mg mirtazapine, there were no (14/17) or only mild (3/17) symptoms. In 21 children ingesting 30–45 mg, 14 showed no symptoms and 7 had symptoms including somnolence and bradycardia (55/min). Ingestion of  $\geq 60$  mg mirtazapine caused symptoms in the majority of toddlers (7/12), such as impaired consciousness, agitation or tachycardia. In adolescents (14–< 18 years, n = 30) and adults (18–< 65 years, n = 367) at doses < 400 mg there were no symptoms in  $\geq 50\%$ . The most frequent symptoms were neurological (drowsiness/dizziness/somnolence, vertigo), gastrointestinal (nausea, vomiting) and cardiovascular (tachycardia). At doses  $\geq 600$  mg at least 40% were somnolent and in single cases fasciculations and rhabdomyolysis occurred. At doses up to 900 mg mirtazapine the frequency of symptoms increased up to 75% but remained predominantly mild. Coma, cramping, seizures, hypotension, hypertension and hypokalaemia were among the symptoms reported at doses  $\geq 900$  mg. In elderly adults ( $\geq 65$  years, n = 25) symptoms occurred more frequently and also at a lower dose starting at 75 mg (most common: somnolence). **Conclusion:** In children aged 1–< 6 years no or only mild symptoms can be expected at mirtazapine overdose up to 15–30 mg. In adolescents and adults severe symptoms have to be expected at doses  $\geq 900$  mg. Elderly people are more susceptible with symptoms occurring more frequently at  $\geq 75$  mg mirtazapine. **Reference:** 1. 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 (Phila)* 2007; 45:45–50.

#### 195. Acute Toxicity Profile of Paliperidone in Overdose: A Multicentre Consecutive Case Series

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**Objective:** Paliperidone (9-hydroxyrisperidone) is the major active metabolite of the second-generation antipsychotic risperidone. Its mechanism of action is thought to be the antagonism of dopamine D<sub>2</sub> and serotonin 5-HT<sub>2A</sub> receptors. The aim of the study was to analyse the clinical features of paliperidone poisoning, since information on patterns of toxicity of this substance in overdose is scarce, and limited to case reports. **Methods:** A multicentre retrospective consecutive review of acute

**Table 1.** Signs and symptoms in paliperidone overdoses.

Symptom/Sign	Severity	
	Minor	Moderate
Somnolence	7 (50%)	
Dystonic reactions	3 (21%)	2 (14%)
Restlessness	1 (7%)	
Disorientation		1 (7%)
Tachycardia		
100–139 bpm	6 (43%)	
140–179 bpm		2 (14%)
Hypotension	3 (21%)	
ECG changes - mild (QTc 390–430 ms <sup>♂</sup> , 440–485 ms <sup>♀</sup> , extra systoles, RBBB)	1 (7%)	
Miosis	1 (7%)	

paliperidone monointoxications involving adults and reported by physicians to German, Austrian, and Swiss PCs between January 2006–December 2010. **Results:** Nine (64%) females, 4 (29%) males, and 1 case with unspecified gender could be included. Mean age was 29 years (range 20–47). The ingested dose ranged from 24 to 375 mg (mean 115 mg). One (7%) patient remained asymptomatic, 9 (64%) showed minor, and 4 (29%) moderate symptoms (PSS). There were no severe or fatal cases. Minor symptoms occurred after ingestion of 45 to 375 mg paliperidone (mean 150 mg), and moderate symptoms with 24 to 90 mg (mean 53 mg). Signs and symptoms predominantly involved the central nervous and the cardiovascular systems (Table 1). In 8 cases symptoms persisted longer than 24 h, with a maximum duration of 70 h in one case. **Conclusion:** The severity of poisoning was not related to the ingested paliperidone dose. In this study, paliperidone overdose was associated with transient, mild to moderate, neurological and cardiovascular signs/symptoms. The incidence of dystonic reactions seems to be higher compared to risperidone. Due to the osmotic drug-releasing technology, symptoms can persist for > 24 h, but complete recovery can be expected with supportive care.

#### 196. Pediatric Clotiapine Poisoning: Clinical Manifestations and Toxicokinetics

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**Objective:** Clotiapine is an antipsychotic drug commonly used in Europe and in Israel. There is limited information concerning the clinical manifestations of clotiapine poisoning and there are no pharmacokinetic or toxicokinetic data. We report the clinical manifestations and toxicokinetics of a pediatric clotiapine poisoning. **Case report:** An 18 month old toddler was brought to the hospital two and a half hours after ingesting clotiapine tablets; five 40 mg tablets were missing. On admission, she was stuporous, with Glasgow Coma Scale 9, miosis, pulse 90/minute, blood pressure 130/70 mmHg, O<sub>2</sub> saturation 100%, and temperature 36.4°C. Arterial blood gases, complete blood count and biochemistry values were within normal limits. Serial clotiapine plasma levels measured by liquid chromatography tandem mass spectrometry gradually decreased from 128 ng/mL 22 hours after ingestion to 9 ng/mL 60 hours after ingestion. Plasma

clotiapine half life calculated using linear regression was 9.8 hours. She was hospitalized in the intensive care unit, treated supportively, and recovered completely within 36 hours. **Conclusion:** We report a case of pediatric clotiapine overdose. The main clinical manifestation was CNS depression. Clotiapine plasma levels 22–60 hours after ingestion were in the range reported in adult patients treated with 20–220 mg/day (7.7–148 ng/mL, respectively).<sup>1</sup> Clotiapine half life in our patient was 9.8 hours; no similar data have been reported in either children or adults. Clotiapine is an antipsychotic agent displaying anticholinergic and antiserotonergic properties. In animal models it was also found to be a noncompetitive antagonist of norepinephrine, dopamine and histamine.<sup>1</sup> The main adverse effects are neurological, especially extrapyramidal signs; neuroleptic malignant syndrome was also reported.<sup>2</sup> Meticulous monitoring for at least 24 hours and supportive treatment are recommended. **References:** 1. Sporkert F, Augsburger M, Giroud C, et al. Determination and distribution of clotiapine (Entumine) in human plasma, post-mortem blood and tissue samples from clotiapine-treated patients and from autopsy cases. *Forensic Sci Int* 2007; 170:193–9. 2. Abu-Kishk I, Toledano M, Reis A, et al. Neuroleptic malignant syndrome in a child treated with an atypical antipsychotic. *J Toxicol Clin Toxicol* 2004; 42:921–5.

#### 197. Prolonged Toxicity and Respiratory Arrest Following Phenytoin Overdose

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**Objective:** To describe a case with a substantially delayed peak phenytoin concentration associated with severe clinical effects following overdose. **Case report:** A 57 year old epileptic male patient was admitted following an acute overdose of phenytoin up to 13 g. Initial features included agitation, confusion, ataxia and nystagmus. The phenytoin concentration on admission was 32 mg/L. CT head scan and other relevant bloods were unremarkable. No activated charcoal was given, due to unsafe swallowing. The patient was managed conservatively; including sedation with intermittent haloperidol and benzodiazepines. The day after admission his clinical features had improved but 3 days after admission he developed sudden respiratory arrest. No convulsions or arrhythmias were noted. No sedation had been given in the preceding 12 hours. Spontaneous ventilation was restored by basic life support. He was in sinus rhythm and haemodynamically stable with Glasgow Coma Scale 11–13/15, normal pupils, nystagmus, normal tone and downgoing plantar responses. A chest X-ray was normal as were acid base status, liver and renal function. The phenytoin concentration, however, had increased to 49 mg/L. On the 6th day after admission the phenytoin concentration was 27.6 mg/L. The patient continued to improve and was discharged 9 days after admission. **Conclusion:** The clinical features observed suggest a recrudescence of phenytoin toxicity 3 days after admission associated with an increased phenytoin concentration. The explanation for this is uncertain; delayed absorption has been reported in a previous case and there may be a contribution from the complex and variable pharmacokinetics of phenytoin and prolonged elimination after poisoning.<sup>1,2</sup> There was no evidence of further consumption of phenytoin in hospital or administration of interacting drugs. This case provides further

evidence that delayed toxicity may occasionally occur after phenytoin ingestion. *References:* 1. Chua HC, Venketasubramanian N, Tjia H, et al. Elimination of phenytoin in toxic overdose. *Clin Neurol Neurosurg* 2000; 102:6–8. 2. Chaikin P, Adir J. Unusual absorption profile of phenytoin in a massive overdose case. *J Clin Pharmacol* 1987; 27:70–3.

### 198. Seizures and Rhabdomyolysis in a Doxylamine Poisoning

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*Objective:* Doxylamine succinate, an over-the-counter ethanalamine-based antihistamine, used as a night-time sleep aid, can cause severe anticholinergic effects at toxic doses, including seizures, rhabdomyolysis and death. We present a case of severe doxylamine overdose in which instead of high plasma concentration, we limited the toxic effects with adequate therapy. *Case report:* A 29 year old woman, with aplastic anemia was admitted following suicidal ingestion of 90 tablets (1 tablet = 25 mg, total dose = 2.25 g, BW = 55 kg) of a doxylamine over-the-counter medication bought from the Internet (not approved in our country). The emergency physicians found her at home confused and agitated, 2 hours after ingestion; soon after she developed seizures with coma. On admission: sedated and intubated patient, fixed equal mydriasis, flushed and dry skin, normal pulmonary sounds, hypertension, non-invasive BP = 140/80 mmHg, tachycardia 136 b/min., hyperthermia 38°C, dark coloured urine. Initial abnormal findings: myoglobin 482.3 micrograms/L, creatine kinase (CK) 3500 U/L, lactate dehydrogenase (LDH) 842 U/L. Toxicology analysis by GS/MS was positive for doxylamine in urine. The first GS/MS urine test (SIS method) at 4 hours from ingestion showed doxylamine 8.58 mg/L with 2 metabolites (M1 – carbinol-doxylamine = 0.77 mg/L and M2 – nor-doxylamine = 0.05 mg/L); the second test at 16 hours from ingestion: doxylamine 84.6 mg/L with 2 metabolites (M1 = 14.5 mg/L, M2 = 3.78 mg/L). The plasma concentrations of doxylamine were 2.08 mg/L at 16 hours, 1.875 mg/L at 24 hours, 0.904 mg/L at 32 hours. The therapy initiated was ventilatory support, sedation with benzodiazepines, aggressive intravenous fluid replacement and forced alkaline diuresis. Gastric lavage was performed and a 50 g dose of activated charcoal was administered. The outcome was favourable. Myoglobin, CK, LDH decreased, renal function remained normal. The patient was weaned from ventilator support after 3 days and discharged to a psychiatric institution after 7 days, with normal laboratory tests. *Conclusion:* Antihistamine overdose is a life-threatening situation and needs fast treatment to avoid complications. The patient can be managed successfully, even if the ingested dose is larger than 20 mg/kg, if the physicians are aware of the multiple receptor and organ effects.

### 199. Global Aphasia after Diclofenac? A Rare Case of Drug Induced Acute Porphyria with Persistent Neuropsychiatric Sequelae

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*Objective:* Neuropsychiatric alterations due to acute porphyria are common. However, occurrence of global aphasia after diclofenac-induced acute porphyria to our knowledge has never been reported before. *Case report:* A 21-year old female patient was treated for lumbago with diclofenac and tetrazepam. Two days later she complained of persistent dorsalgia and abdominal pain and was admitted to hospital. At that time psychomotor agitation was already present calling for lorazepam and haloperidol and abdominal pain only partially resolved after administration of flupirtine and metamizole. Consciousness worsened two days later and a cerebral CT-scan showed generalized cerebral edema. EEG excluded convulsions and cerebrospinal fluid (CSF) was normal but severe hyponatremia in serum was present (109 mmol/L). A Schwartz-Bartter-syndrome or a syndrome of inappropriate antidiuretic hormone hypersecretion (SIADH) were primarily considered as differential diagnoses but could be excluded. The patient was transferred with finally suspected acute porphyria. Subsequent measurements of levels of porphyrins in a 24h-urine sample confirmed the diagnosis of acute intermittent porphyria with extremely elevated total porphyrins (786 µg/24h), porphobilinogen (29.3 mg/24h), coproporphyrin (255 mg/24h) and marginally elevated Δ-aminolaevulinic acid (6.6 mg/24h). Treatment comprised a cautious sodium-substitution, supportive therapy, a high carbohydrate diet and IV hematin over 4 days. In the clinical course her condition slowly improved so that the patient was able to eat and walk on her own. However, she had difficulties in communicating with both receptive and expressive aphasia. Magnetic resonance imaging on day 25 (which she could not tolerate before) showed abnormal cortical contrast enhancement and edema of almost the entire left hemisphere, and the right temporal region, as well as in the subcortical left frontal and temporal lobe consistent with her global aphasia. The patient improved over the next 14 days so that she was able to follow simple commands and to verbally express single words. However, despite speech therapy, a severe central speech disorder was still present when she was able to be transferred for neuropsychiatric rehabilitation. *Conclusion:* In this case, diclofenac was considered as the most likely trigger for acute intermittent porphyria. SIADH with hyponatremia may have complicated the course. Beside common neuropsychiatric manifestations of porphyria, global aphasia may be an extreme rare, but plausible manifestation calling for thorough diagnostic and therapeutic approaches.

### 200. A Survey of Adverse Drug Reactions Based on Data from a Toxicology Unit

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*Objective:* There is a wide variation of adverse drug reaction (ADR) related admissions among different studies worldwide. Incidence of ADRs in Bulgaria is still difficult to monitor. Although the Bulgarian Drug Agency created a system for the reporting and monitoring of such cases, they are still under-reported, especially when patients are treated by general practitioners or at non-specialized departments at local/regional hospitals. A pilot study of ADR-related hospitalizations (frequency, severity and main causes) in toxicology units was carried out. A brief overview of country specific regulations and reporting systems with their advantages and disadvantages is presented, as

well as recommendations for improvements. *Methods:* We studied retrospectively medical records of patients with ADR-related hospitalizations at the Toxicology Clinic, Sofia for a two year period and at the Toxicology Unit of regional hospital in Pleven for 10 months. *Results:* 5123 patients were treated at the Toxicology Clinic, Sofia between 2007 and 2009. 23.2% of these were hospitalized due to ADR. Leading causative agents were: non-steroidal anti-inflammatory drugs NSAIDs (9.9%), antibiotics (8.2%), ACE-inhibitors (3.4%), other drugs – metoclopramide, x-ray contracts agents, anticonvulsants, etc (1.7%). Age and gender prevalence differed between various types of causative agents: male gender prevailed among ACE-inhibitor ADRs (58%), while females prevail among NSAIDs-related ADRs. Moderate ADRs prevailed, accounting for 68% of cases. All patients recovered and were discharged healthy. In 30% of cases the ADR which appeared at the point of hospitalization had occurred previously on at least one occasion. The survey at the Toxicology Unit, UMHAT Pleven, started in 2011 and until end of October 32 patients were hospitalized as the result of ADRs. Most frequently ADRs were caused by antibiotics (14 patients), followed by ‘other drugs’ (13 patients); NSAIDs (5 patients). Sixty-seven per cent were children up to 18 years of age. Seven of the children (37%) were hospitalized due to ADR to metoclopramide. Clinical presentation of ADRs varied among skin rashes; gastrointestinal symptoms, including bleeding; extrapyramidal syndrome; angioedema. *Conclusion:* Incidence of ADR is unknown due to incompleteness of data. Further studies to identify incidence of ADRs and ADR-related hospitalization are required. Spontaneous ADR reporting should be encouraged and improved. Educational courses among general practitioners would be beneficial for improving ADR monitoring.

### 201. Fetal Outcomes Following Dosulepin Overdose in Pregnancy

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*Objective:* Dosulepin is a tricyclic antidepressant used in the treatment of depressive illness. There are no published data describing fetal outcomes following overdose of dosulepin in pregnancy, and data on therapeutic use are limited.<sup>1,2</sup> The UK Teratology Information Service (UKTIS) continually aims to collect pregnancy outcome data to assess the potential teratogenicity of dosulepin overdose during pregnancy. *Methods:* Using standardised procedures, UKTIS provided risk assessment and collected outcome data on 42 prospective cases of dosulepin overdose during pregnancy. Overdose was defined as documented ingestion of more than the maximum daily therapeutic amount (225 mg). *Results:* There were 42 cases of dosulepin overdose, with reported doses ranging from 300 mg to 2 g (median ingested dose: 750 mg). Of these 30 (71%) were exposed to other medications in overdose or therapeutically. First trimester exposure occurred in 19 cases, second trimester exposure in 12 cases and third trimester exposure in six. The stage of pregnancy at exposure was unknown in five cases. No major congenital malformations were observed in the 29 live-born infants (0/29, 0%; 95% CI 0 to 14.5). Neonatal problems

were reported in two infants; one was jaundiced at birth, and one baby had a small umbilical hernia. Other outcomes included nine elective terminations, three spontaneous abortions and one maternal death with associated intrauterine death. **Conclusion:** These limited UKTIS data do not indicate an increased risk of congenital malformations or any specific type of defect, however small increases in overall risk or in the risk of specific malformations cannot be excluded given the limited data available. **References:** 1. McElhatton PR, Garbis HM, Elefant E, et al. The outcome of pregnancy in 689 women exposed to therapeutic doses of antidepressants. A collaborative study of the European Network of Teratology Information Services (ENTIS). *Reprod Toxicol* 1996; 10:285–94. 2. Prentice A, Brown R. Fetal tachyarrhythmia and maternal antidepressant treatment. *BMJ* 1989; 298:190.

## 202. Fetal Outcomes Following Fentanyl Exposure in Pregnancy

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**Objective:** Fentanyl is a potent synthetic opioid analgesic approximately 100 times more powerful than morphine. Use near term in pregnancy has been associated with neonatal withdrawal symptoms<sup>1,2</sup> and muscle rigidity in the neonate<sup>3,4</sup>, but there are no published data regarding the teratogenic risk after *in utero* exposure to fentanyl. This on-going prospective case series aims to collect data with which to assess potential fetotoxic effects of fentanyl exposure during pregnancy. **Methods:** The UK Teratology Information Service collected outcome data on a prospective case series of 17 exposures to fentanyl in pregnancy. **Results:** First trimester exposure occurred in 14 cases and second trimester exposure in one case; no details on stage of pregnancy at exposure were available for the remaining two cases. The outcomes were 13 live-born infants, three elective terminations and one spontaneous abortion. No major congenital malformations were observed in the 13 live-born infants (0/13, 0%; 95% CI 0 to 28.3). Neonatal problems were reported in two infants; one baby experienced fetal distress and required observation in neonatal intensive care for 24 hours; the other required monitoring on a special care unit for three weeks. Timing of exposure in both these cases was unavailable. **Conclusion:** As previously reported with opioids, fentanyl exposure during pregnancy may be associated with neonatal withdrawal and respiratory distress.<sup>1,2</sup> UKTIS data does not indicate an increased risk of major congenital malformations or of any specific type of defect. However, due to the limited data available, a teratogenic risk cannot be excluded. **References:** 1. Regan J, Chambers F, Gorman W, et al. Neonatal abstinence syndrome due to prolonged administration of fentanyl in pregnancy. *BJOG* 2000; 107:570–2. 2. Cohen RS. Fentanyl transdermal analgesia during pregnancy and lactation. *J Hum Lact* 2009; 25:359–61. 3. Eventov-Freeman S, Rozin I, Shinwell ES. Case of chest-wall rigidity in a preterm infant caused by prenatal fentanyl administration. *J Perinatol* 2010; 30:149–50. 4. Lindemann R. Respiratory muscle rigidity in a preterm infant after use of fentanyl during Caesarean section. *Eur J Pediatr* 1998; 157:1012–3.

## 203. Sildenafil Related Deaths in The Netherlands

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**Objective:** To compare the recently reported impressive number of sildenafil related deaths from the files of the Center for Drug Evaluation and Research of the FDA<sup>1</sup> with the files of our institute (The Netherlands Forensic Institute). **Methods:** We reviewed the files of The Netherlands Forensic Institute for possible drug-related deaths (direct and indirect), where the presence of sildenafil was demonstrated in blood. **Results:** From 2005–2011, we found 16 possibly relevant cases out of 2213 forensic autopsies. In 4 of these cases, we concluded that sildenafil contributed to death. Sildenafil was never the sole agent. Gamma-hydroxybutyrate (GHB) and cocaine were present in 2 out of the 4 cases. Other compounds were ethanol, amphetamines, cannabis, olanzapine and khat. Concentrations of sildenafil in femoral blood varied from 0.06 to 0.31 mg/L (n = 3). In the other 12 cases, sildenafil was present in blood at a low concentration, or its relative contribution to death was deemed irrelevant. In these cases, amphetamines were present in blood in 9 out of 12 cases. Other compounds present were cocaine (4/12), ethanol (3/12), GHB (3/12), benzodiazepines (2/12), cannabis (2/12), ketamine (2/12), tramadol, fluvoxamine, mirtazapine, quetiapine, nortriptyline and methylphenidate (all 1/12). **Conclusion:** Sildenafil does not seem to play an important role in drug-related deaths in The Netherlands. However, the frequent concomitant presence of stimulants in cases where sildenafil was demonstrated points to a possible contributory role of sildenafil in these cases, even at low concentrations. **Reference:** 1. Lowe G, Costabile RA. 10-Year analysis of adverse event reports to the Food and Drug Administration for phosphodiesterase type-5 inhibitors. *J Sex Med* 2012; 9:265–70.

## 204. Xtreme Hepatotoxicity: Prolonged Cholestatic Hepatitis due to Ingestion of “Natural” Bodybuilding Supplement

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**Objective:** Multiple bodybuilding supplements are sold over the counter under the premise that they are natural and therefore safe. We describe a case of profound cholestatic hepatitis that developed after the use of a “natural” product purchased from a health food store, which was found to contain anabolic androgenic steroids (AAS). **Case report:** A 20 year-old previously healthy man presented to the emergency department with jaundice, right upper quadrant abdominal (RUQ) pain, and pruritus. One week prior to presentation he had completed a four-week course of a bodybuilding supplement labeled “Tri-methyl Xtreme,” which he purchased as a “safe and natural” steroid precursor. The product was identified as containing the AAS methasterone (2a,17a-di-methyletiocholan-3-one, 17d-ol), methoxydienone (13-ethyl-methoxy-gona-2,5(10)dien-17-one), and 2a,3a-epithio-17a-methyl-5a-androstane-17b-ol, in addition to vanadyl sulfate, and extracts of *Tribulus terrestris* and *Eurycoma longifolia*. He denied use of alcohol, illicit substances, or other medications. Upon arrival he was hemodynamically stable with marked jaundice and mild RUQ tenderness. His initial laboratory analysis revealed: total bilirubin, 173.4 μmol/L; direct bilirubin, 119 μmol/L; aspartate aminotransferase (AST),

133 U/L; alanine aminotransferase (ALT), 349 U/L; alkaline phosphatase, 97 U/L; and INR, 1.0. No bile duct obstruction was found on ultrasound or magnetic resonance cholangiopancreatography. An extensive evaluation for other causes of hepatitis was negative. Sixteen days after initial presentation his total and direct bilirubin peaked at 683.4 μmol/L and 426.7 μmol/L. AST and ALT remained minimally elevated. He was started on ursodeoxycholic acid (ursodiol) on day 13, and had a progressive decline in bilirubin. **Conclusion:** AAS are commonly used for body building. Despite their classification as controlled substances, multiple AAS-containing compounds are illegally available for purchase over-the-counter and online, and are often misrepresented as natural products. The pattern of cholestatic hepatitis demonstrated by this case is typical of the liver injury induced by 17-alpha alkylated agents, which is characterized by dramatically elevated bilirubin and mild transaminase elevation. Ursodiol may be a useful treatment adjunct in cases of AAS-induced cholestasis. The use of AAS in the form of over-the-counter body building supplements may result in prolonged cholestatic hepatotoxicity. Early recognition of this entity could allow for prompt diagnosis, education, and prevention.

## 205. Promethazine Use among Methadone Patients: Implications for Increased Risk of Torsade de Pointes

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**Objective:** Promethazine has been reported to be misused in conjunction with opioids in several settings. To date, no prevalence data for the nonmedical use of promethazine has been reported. Promethazine use alone or in conjunction with opioids may have serious adverse effects. Promethazine prolongs the QT interval. If promethazine is misused in combination with methadone this could result in a significant increased risk for torsade de pointes. The objective of this study was to determine the prevalence of promethazine use in two different populations: methadone maintenance clinic patients and community-based injection drug users (IDUs). **Methods:** A LC-MS/MS method was developed and validated for the determination of promethazine in urine. Promethazine 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 urines collected for drug screens at a methadone maintenance clinic (N = 334) were tested for promethazine for one month. In addition, targeted sampling methods were used to recruit and survey 200 community-based IDUs about their use of promethazine. We assessed prevalence and factors associated with promethazine use with bivariate and multivariate statistics. **Results:** The prevalence of promethazine positive urine samples among the methadone maintenance patients was 26%. Only 15% of the promethazine positive patients had an active prescription for promethazine. Among IDUs reporting injection of opiates in the community-based survey, 17 per cent reported having used promethazine in the past month, while 24% of the IDUs who reported being enrolled in methadone treatment reported using promethazine in the past month. **Conclusion:** The finding that one quarter of methadone maintenance patients in a clinic or recruited in community settings has recently used promethazine provides compelling evi-

dence of significant nonmedical use of promethazine in this patient population. Clinicians and Poison Control Center professionals should be aware of promethazine misuse among methadone patients and the possible serious adverse effects that could result from misusing the two drugs in combination. Further studies are underway to elucidate the increased health risks associated with the combined use of methadone and promethazine.

#### 206. Acute Amikacin Overdose in a Neonate

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**Objective:** Amikacin is an aminoglycoside frequently used in neonates. Although nephrotoxicity and ototoxicity are well-known complications of long-term treatment, limited experience of acute overdose is available in neonates. Our aim is to describe the outcome and toxicokinetics following a 10-fold overdose of amikacin. **Case report:** A 7-day-old full-term neonate weighing 2,880 g was admitted in the emergency paediatric department for fever (39°C). As group B Streptococcus colonization was documented during pregnancy, a combined treatment with amikacin (45 mg) and cefotaxime (100 mg every 8 hours) was started pending culture results. The neonate was mistakenly administered 450 mg amikacin (156 mg/kg over 1 hour). The dosing error was detected only 12 hours later and careful rehydration was immediately initiated. Amikacin levels measured 14, 23 and 48 hours after the accidental administration were 30.6 mg/L, 12.9 mg/L and less than 2 mg/L, respectively. Extrapolated peak level at the end of amikacin perfusion was estimated at 224 mg/L. Serum creatinine (34 µmol/L), blood urea nitrogen (2.9 mmol/L) and serum electrolyte levels remained unchanged during the 2-day period of follow-up. Otoacoustic emissions performed 3 days after the overdose were normal and auditory evoked potentials measured on day 23 were considered subnormal (thresholds were 40 dB on right ear and 50 dB on left ear). Although long term auditory and renal follow-up is still pending, the mother stated that her infant, now aged 15 months, normally reacted to acoustic stimuli. **Conclusion:** To our knowledge this is the highest overdose resulting from aminoglycoside administration ever published in a neonate. Previous paediatric reports mentioned that hemodialysis rapidly cleared gentamicin in a 14-month-old girl who had received 56 mg/kg, whereas the usefulness of peritoneal dialysis has been challenged in 3 other infants as only a marginal increase in gentamicin removal was observed after accidental overdose (19 to 40 mg/kg). Another report identified no immediate renal or auditory consequences in a preterm infant exposed to a 10-fold overdose of gentamicin and treated with only slightly increased fluid intake. Accordingly, we suggest that increased fluid intake may be sufficient to manage massive amikacin overdose in infants.

#### 207. Two Cases of Isoniazid Induced Hepatotoxicity in Children: Treatment with N-Acetylcysteine

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**Objective:** Hepatotoxicity is a rare, potentially fatal complication of isoniazid (INH) therapy. Although the cornerstone of treatment is immediate cessation of INH, some data suggest a protective effect of N-acetylcysteine (NAC). We report two cases of INH hepatotoxicity in children with temporal improvement following NAC administration. **Case series:** Case One. A 12 year-old girl presented to the ED with nausea, vomiting, abdominal pain, and jaundice. She took INH 300 mg daily for seven months for latent tuberculosis (TB). Routine laboratory evaluation three days prior revealed AST 1329 IU/L and ALT 1079 IU/L but INH was not discontinued. ED Laboratories revealed: AST 1928 IU/L; ALT 1352 IU/L; bilirubin 5.7 mg/dL, and INR 1.5. Serum acetaminophen (APAP) was undetectable. Viral hepatitis serologies and liver hepatic ultrasound were unremarkable. There was no history of exposure to other hepatotoxins. INH was discontinued. On HD2, she remained symptomatic with: AST 1927 IU/L; ALT 1374 IU/L; INR 1.25; and bilirubin 7 mg/dL. On HD3, continuous IV NAC was started. By HD4, she improved: AST 1515 IU/L; ALT 1002 IU/L; bilirubin 6 mg/dL. She received NAC until discharge (HD10) with continued improvement. One-week later: AST 445IU/L; ALT 290IU/L; bilirubin 3.3 mg/dL, INR normal. Case Two. A six-year old girl presented to clinic with asymptomatic jaundice for 6-weeks after taking INH 200 mg daily 8-weeks. Laboratories revealed: AST 2130 IU/L; ALT 1834 IU/L; bilirubin 11 mg/dL; and INR 1.37. INH was stopped and 3 days later laboratories transiently improved: AST 1489 IU/L; ALT 1361 IU/L; bilirubin 9.5; and INR 1.08 mg/dL. Three-days following discharge repeat laboratories were: AST 1968 IU/L; ALT 1493 IU/L. Serum APAP was undetectable, viral hepatitis serologies and liver hepatic ultrasound were unremarkable. There was no history of exposure to other hepatotoxins. With 3 days of continuous IV NAC she improved: AST 1669 IU/L; ALT 1334 IU/L; bilirubin 7.3 mg/dL; and INR 1.03. Nine days after discharge: AST 397 IU/L; ALT 712 IU/L; bilirubin 2.4; and INR normal. **Conclusion:** NAC is a safe therapy that provides hepatic protection from hepatotoxins. Though rare, children taking INH can develop hepatotoxicity. NAC should be considered in those that fail to improve with INH cessation.

#### 208. Cardiovascular Collapse Following an Intravenous Azithromycin Overdose in an Infant

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**Objective:** Azithromycin is a common and safe antibiotic in children and adults. We report a bradycardic cardiac arrest following an intravenous overdose of azithromycin in an infant. **Case report:** A six month-old boy presented to the emergency department with fever and cough for one week. Initial vital signs: BP, 80/46 mmHg; HR, 112 beats/min; RR, 41 breaths/min; T, 38.4°C; SpO<sub>2</sub>, 96%RA, weight, 8 kg. On examination, he was alert, with mild respiratory distress and right-sided chest rhonchi. The remainder of the examination was unremarkable. Standard blood chemistries and a complete blood count (CBC) were normal. Chest x-ray showed a small pulmonary infiltrate and both ceftriaxone and azithromycin were ordered. The patient received ceftriaxone 50 mg/kg IV without sequelae. During the infusion of the azithromycin it was identified that a dose of 500 mg IV was ordered rather than 80 mg, and the infusion was interrupted after approximately 80% was infused. Twenty-five minutes later,

the patient was noted to be cyanotic and listless and was bradycardic and hypotensive. Pediatric Advanced Life Support (PALS) was performed and several doses of epinephrine and atropine resulted in only transient improvements in his heart rate and perfusion. Following approximately forty minutes of resuscitation, the patient regained pulses but remained unresponsive. Supportive care ensued until three days later when his brain perfusion scan was consistent with brain death and he expired. **Conclusion:** While the manufacturer's instructions for intravenous azithromycin indicate no safe dose for children, hospitals routinely administer intravenous azithromycin 10 mg/kg to pediatric patients off-label. This patient received approximately a six-fold overdose (62.5 mg/kg). Macrolide cardiotoxicity is typically associated with prolonged QT and torsade de pointes, which this patient never developed. Rather, the cardiovascular collapse was strikingly similar to a previously reported infant<sup>1</sup> and in adults exposed to the veterinary macrolide antibiotic, tilmosin.<sup>2</sup> Although there is no clear mechanism for this complication, calcium channel blockade is suggested and calcium salts have been used as an antidote. **References:** 1. Tilelli JA, Smith KM, Pettignano R. Life-threatening bradyarrhythmia after massive azithromycin overdose. *Pharmacotherapy* 2006; 26:147–50. 2. Veenhuizen MF, Wright TJ, McManus RF, et al. Analysis of reports of human exposure to Micotil 300 (tilmosin injection). *J Am Vet Med Assoc* 2006; 229:1737–42.

#### 209. Pediatric Lidocaine Toxicity Following Intraosseous Injection: A Case Series

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**Objective:** To describe two cases of lidocaine toxicity following inadvertent intraosseous overdose presenting to the same pediatric intensive care unit (ICU) on the same day. **Case series:** Patient #1: An 11 month old male presented to a rural hospital for respiratory distress. An intravenous (IV) line was established and he was given an IV fluid bolus started on ceftriaxone, and admitted to the pediatric ward. His condition worsened throughout the evening, his IV access was lost, and he was transferred to the adult ICU (no local pediatric ICU available). An intraosseous (IO) line was established and, to ease the pain of subsequent injections, 10 mL of 1% lidocaine (10.1 mg/kg) was administered as a bolus. Within minutes he developed a tonic-clonic seizure which lasted approximately 18 minutes. He was given 0.1 mg/kg of lorazepam and a bolus of intralipid (12 mL of 20% solution) via the IO line. An intralipid drip was initiated through the same IO line but was discontinued prior to transfer to a tertiary facility. He had no further seizures and recovered uneventfully. Patient #2: A 6-month old male presented to a rural hospital for intractable vomiting, diarrhea, and fever. Several attempts at IV access were unsuccessful. An anesthesiologist was consulted and placed an IO line. The skin was first anesthetized with 0.2 mL of 1% lidocaine (0.22 mg/kg), and, once bone marrow was cannulated, the line was flushed with 4 mL of 1% lidocaine (4.5 mg/kg). Within 40 seconds, the child experienced a generalized tonic-clonic seizure lasting 30 seconds. He was transferred to the same tertiary facility, where he also recovered uneventfully without further seizures or cardiovascular effects. **Conclusion:** While complications from IO lines are infrequent,<sup>1</sup> these cases illustrate that medications administered via the intraosseous route may result in systemic toxicity and reinforce the need for judicious confirmation of appropriate dosing in pediatric patients. **Reference:** 1. Hansen M,

Meckler G, Spiro D, et al. Intraosseous line use, complications, and outcomes among a population-based cohort of children presenting to California hospitals. *Pediatr Emerg Care* 2011; 27:928–32.

### 210. Application of Potentially Corrosive Vortex R Drops Instead of Vitamin-D Drops Orally in Small Children

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**Objective:** To describe a series of cases where Vortex R and Vitamin-D were confused in order to assess the damage caused and to identify means of preventing similar medication errors. **Case series:** Five cases, received by the Danish Poison Information Centre “Gifflinjen” over a time period of 5.5 years: 1. A boy, 3 weeks old, was brought to an emergency department after his parents by accident administered 4 drops of Vortex R in his mouth instead of Vitamin-D drops. Symptoms: “Refuses to drink, otherwise unaffected”. 2. A girl, 4 months old, was brought to an emergency department after her father had dripped Vortex R in her mouth instead of Vitamin-D. Maximum 2 mL were administered and the father removed the drug with a towel. The girl was breastfed before going to the hospital. Symptoms: “Small, white linings on the oral mucosa”. 3. A girl, 10 months old, was given Vortex R orally by her mother instead of Vitamin-D drops. Afterwards the child was given water to drink. The mother described: “White elements in the oral cavity, no other inconveniences”. 4. A boy, 0–3 months old, was given Vortex R instead of Vitamin-D. The mother washed his mouth with water. Afterwards he was crying and had “white spots around the mouth and on the tongue”. 5. A girl, 3 months old, was given Vortex R by her mother instead of Vitamin-D drops. The mother described her daughter’s tongue: “Changed colour, not swollen”. A paediatrician later saw the child in the emergency department. Symptoms: “Well and babbling”. Superficial white, peeling elements found in the mouth, on one of the tonsils and on the lips. No deep corrosions. Red spots on the chin. **Conclusion:** Vortex R is an over-the-counter drug for topical treatment of warts and corns. It contains collodion, lactic acid and salicylic acid. The pH is uncertain. No serious corrosive features appeared. Like vitamin-D Drops for children, this product is available in brown 10 mL-bottles with white caps. To prevent confusion, parents should be advised to keep Vitamin-D drops separated from other medications in similar bottles.

### 211. Accidental Ocular Administration of Non-Ocular Pharmaceuticals

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**Objective:** To describe cases of ocular dosing of non-ocular pharmaceutical products reported to an Australian poisons centre. Medication administration errors are well known to contribute to morbidity in the community. Wrong route errors are well documented from parenteral administration of oral liquid preparations, less is known about ocular administration of non-ocular products. **Methods:** A retrospective review of calls made to the NSW Poisons Information Centre (the largest poisons centre of the Australian network) during 2004–2010 involving accidental ocular administration of non-ocular therapeutic products. **Results:** 800 cases were found over this time

**Table 1.** Top 10 non-ocular products administered into the eye.

Product name	Active ingredient	Number of cases
Elocon Lotion	Mometasone	125
Betadine Antiseptic Liquid	Povidone-iodine	82
Aquaear Ear Drops	Acetic acid, isopropyl alcohol	61
Canesten Solution	Clotrimazole	46
Kenacomb Otic Ear Drops	Triamcinolone, neomycin, gram-icidin, nystatin	30
Novasone Lotion	Mometasone	27
Resolve Solution	Miconazole	26
Waxsol Ear Drops	Docusate	23
Otocomb Otic Ear Drops	Triamcinolone, neomycin, gram-icidin, nystatin	22
Diprosone Lotion	Betamethasone	19

period. There have been no clear trends over this time period which could be identified. Three-quarters of cases were in adults. The top 10 products mistaken for eye drops and instilled are shown in Table 1. The remaining 43% of cases involved similar products and were predominantly antiseptics, antifungals, antibiotics, ear wax removal, ear drying and nasal decongestant products. There were 22 cases which involved creams, gels or ointments. As a result of eye exposure, 145 cases attended hospital for assessment. **Conclusion:** Accidental administration into the eye of non-ocular pharmaceuticals is common and has remained relatively constant over the past seven years. Further research and revision of product design and packaging needs to be performed to help prevent these therapeutic errors.

### 212. Activated Charcoal Pulmonary Aspiration as Complication from an Inappropriate Treatment of a Patient with Previous Bariatric Surgery after Aldicarb (Chumbinho) Poisoning

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**Objectives:** To report a case of activated charcoal (AC) pulmonary aspiration after poisoning with aldicarb, in a patient with previous bariatric surgery. **Case report:** A 24-y-old man ingested an unknown amount of the illegal rodenticide “chumbinho” (later identified as aldicarb). He was firstly admitted at the local Emergency Room (~30–60 min post-ingestion), showing salivation, myosis, HR = 50/min, and GCS = 15, being treated with atropine 1 mg IV. Gastric lavage (GL) was also performed, and he was then referred to our Emergency Department (ED) 60 min later. Upon admission he remained alert, showing the same cholinergic symptoms plus bronchorrhea; one more dose of atropine (1 mg IV) was given, and continuous infusion with atropine was then started. The ED team decided to perform a new GL, with a small amount of “chumbinho” granules being observed in the lavage samples; in sequence, activated charcoal (AC) was administered through a nasogastric tube. Vomiting (dark aspect) occurred soon after the AC instillation, associated with dyspnea (SpO<sub>2</sub> = 75%), despite the clearing of pulmonary secretions; the patient was then

intubated, with AC being observed in the larynx. A chest radiogram (~4 h post-ingestion) showed gross nodular opacities of acinar type at RSL. His relatives related that he had received bariatric surgery four years earlier (Roux-en-Y gastric bypass), and then became depressed and alcoholic; it was his second suicide attempt. He was discharged at day 12, with no sequelae. Bariatric surgery is a common treatment for severe obesity where conventional treatments have failed. However, a recent retrospective cohort study indicates that though long-term total mortality after gastric bypass surgery is significantly reduced, deaths particularly from diabetes and heart disease, and the rate of death from other causes, such as suicides, is higher in the surgery group. **Conclusion:** A sequence of iatrogenic procedures was performed, and included a second gastric decontamination more than 2 h after ingestion, in a not severely poisoned patient, with no airway protection, and with previous bariatric surgery. This report highlights the potential complications of gastric decontamination in this special group of patients with reduced stomach capacity.

### 213. Evaluation of Toxic Effects after Accidental Oral Administration of Methylergometrine in Infants

Vecchio S, Petrolini VM, Scaravaggi G, Lonati D, Giampreti A, Buscaglia E, Mazzoleni M, Rognoni C, Manzo L, Locatelli CA.

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**Objective:** In October 2011 Methergin® 0.25 mg/mL oral drops (methylergometrine) was withdrawn worldwide due to the large number of therapeutic errors involving children. Methergin® was often administered to the baby instead of other medications (e.g. vitamins, simeticone, acetaminophen). However, the toxic dose has not been established. All cases referred to the Pavia Poison Centre (PPC) of erroneous methylergometrine administration to infants were evaluated in order to identify any toxic effects. **Methods:** A 5-year retrospective study (2007–2011) was performed: all cases of erroneous administration of methylergometrine in infants younger than 5 months, in which the administered dose was known, were evaluated and assessed for sex, age, dose/weight, signs/symptoms. According to pharmacokinetic parameters, the presence of symptoms was evaluated over at least 2 hours after ingestion. **Results:** Seventy-six cases were analyzed (38 M, 38 F; mean age 26.3 days): 14 patients were asymptomatic at least two hours after ingestion (dose ingested 0.035 ± 0.019 mg/kg; mean age 30.7 days) and 19 patients developed symptoms (dose 0.039 ± 0.019 mg/kg; mean age 15.1 days). Signs and symptoms recorded were unexplained crying (13/19; 68%), abdominal pain (10/19; 52.6%), peripheral vasoconstriction/paleness (4/19; 21%), tachycardia (2/19; 10%), and bradycardia (1/19; 5.2%). Severe symptoms (seizures, coma, apnea) were not observed and all patients recovered fully. Analysis of our cases does not show a statistically significant correlation between presence of clinical effects and dose ingested (p = 0.45 Wilcoxon test) or age (p = 0.70 Wilcoxon test). Forty-three patients were asymptomatic at admission (mean time since ingestion: 0.52 hours, range 0.08–1.50 hours – dose 0.026 ± 0.019 mg/kg) but their outcome was unknown. **Conclusion:** Severe clinical manifestations, even fatal events, have been described for accidental parenteral administration of

methylergometrine in newborns or after erroneous administration of oral doses. In our case series, serious effects were not observed (all patients were hospitalized). Withdrawal of the oral drops formulation should avoid exposing patients to serious toxic effects such as those described in published case reports and prevent intoxications. *References:* 1. Tovo S. [Fatal poisoning by Methergin in a newborn infant]. [Article in Italian]. *Minerva Medicoleg* 1961; 81:1–2. 2. Aeby A, Johansson A, De Schuiteneer B, et al. Methylergometrine poisoning in children: review of 34 cases. *J Toxicol Clin Toxicol* 2003; 41:249–53.

#### 214. Oral Chlorhexidine Poisoning in Three Infants

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*Objective:* Chlorhexidine is an antiseptic and antimicrobial drug with bactericidal activity intended for local use. At concentrations above 20% it can be caustic. We describe three newborns who were accidentally given orally 20% of chlorhexidine instead of 30% glucose. *Case series:* Three healthy newborns, a girl and two boys were given, at the age of 1–2 days, in a hospital erroneously 1 ml of 20% chlorhexidine solution instead of 30% glucose solution. The error was detected after two hours. Initial symptoms included vomiting, pain and crying. All babies had coatings and edema of their oral mucous membranes. Other symptoms included drooling, trouble in swallowing, mild burns around mouth and in the oral cavity. One of the boys underwent oesophagoscopy and bronchoscopy on day 2. He had mild burns around the larynx, the epiglottis was erythematous and swollen, the palatine arch had coating and some irritation was detected on the upper oesophageal sphincter. The girl developed coatings and swelling in her mouth in 8 hours. Oesophagoscopy and bronchoscopy performed on the next day showed swelling and coating on epiglottis; the palatine arch and uvula had ulceration. Changes were detected in mucous membranes of her oesophagus and in her stomach large areas of superficial mucous membrane had peeled off. The other boy (1 day old at ingestion) apparently aspirated some of the given chlorhexidine solution. He developed difficulties in breathing with inspiratory stridor while saturation remained normal. He needed extra oxygen (FiO<sub>2</sub> 30–40%). His bronchoscopy showed swelling in the larynx and epiglottis. In the trachea he had swelling of the mucous membranes and coatings down to bifurcation. The first oesophagoscopy was normal, in the second oesophagoscopy, on day 3, the whole oesophagus was covered with coatings that seemed to peel during the procedure. All three babies started recovering after a few days with symptomatic treatment. No permanent sequelae were detected in the boys, the girl remains in follow up for possible development of oesophageal stricture. *Conclusion:* Concentrated (20%) chlorhexidine is caustic and can cause moderate poisoning in newborns after ingestion of a millilitre dose.

#### 215. Iatrogenic Magnesium Poisoning in 8-Week Old Infant with Implanted Permanent Pacemaker

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*Objective:* Case reports about intravenous magnesium intoxication are scarce, especially in infants. *Case report:* An 8-week old girl, 7 weeks after open heart surgery for hypoplastic aortic arch, ventricular septum defect and atrial septum defect repair, and three days after implantation of a pacemaker (Biotronik Evia DR-T; mode DDD) due to complete heart block after the surgery, was transferred from the surgical ward back to the paediatric intensive care unit (PICU) because of apnoeic attacks. On admission she was pale, responsive to touch, febrile 38.2°C, respiratory rate 40/min, SpO<sub>2</sub> 99% on air, heart rate 154/min, normotensive, body weight 4.0 kg. Because of recurrent apnoeic attacks she was intubated and mechanically ventilated soon after admission. Septic workup was done and antibiotic treatment was started. A short cardiac massage was started twice (10 seconds) for two episodes of severe bradycardia (heart rate less than 40/min) despite the pacemaker. A higher electrical threshold of pacemaker was noticed by the consultant cardiologist and the pacemaker was reprogrammed. The first laboratory results revealed a high level of magnesium (8.98 mEq/L). By analysing her medical record, we found that before the admission to PICU she had received ten-times the usual dose of magnesium sulphate (15 mmol) intravenously in 3-hour infusion for treatment of mild hypomagnesaemia (1.1 mEq/L). Calcium gluconate 10% (5 mL) was used as an antidote and levels of magnesium in serum dropped to normal during the next 24 hours (8.98 mmol/L immediately after the infusion of magnesium; 4.62 mEq/L 5 hours after the infusion; 3.40 mEq/L 9 hours after; 2.48 mEq/L 14 hours after; and normal value 1.38 mEq/L 24 hours after). Body temperature dropped to 35.5°C after admission and then normalized with passive measures. She was extubated next day with no recurrent apnoeic attacks or bradycardia. Infection was excluded and antibiotic treatment was discontinued after 36-hours. *Conclusion:* Our case shows that iatrogenic intoxication with magnesium, besides apnoea and bradycardia, can also affect the threshold sensitivity of a pacemaker. Evaluation of previous therapy should always be included in differential diagnosis when experiencing sudden changes in the clinical condition in hospitalized children.

#### 216. Elderly Acute Intoxications in the Emergency Department from 2005 to 2011: Patterns and Outcomes

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*Objective:* Poisoning is the third leading cause of unintentional injury death among people over 65 years old in the European Union.<sup>1</sup> Although morbidity and mortality of acute poisoning is higher in the elderly compared to younger patients, only a few published studies report data on this topic (MEDLINE research). *Methods:* Retrospective study of patients over 65 years of age admitted to the Emergency Department (ED) in Verona (Italy) between Jan 2007 and Oct 2011 for acute intoxication or poisoning. Data examined were age, gender, characteristics of intoxication and admission rates. *Results:* During the study period 1,232 (1.04%) of 118,214 ED admissions of patients aged over 65 years were due to intoxication. The average age was 76 (range 65 – 99) with a slight prevalence of women (53.6%). Intoxications were mostly on an accidental basis (80.2%) rather than intentional and only 44.9% of the patients arrived

by Emergency Medical Service; loss of consciousness was present in 7.3% of the cases. Poisoning was due to concomitant treatment (68.99%), non medical causes (17.05%) and ethanol (13.96%). Drugs responsible for medical intoxication were anticoagulants (34.16%), cardiovascular (11.54%), antihyperglycaemics (8.48%), psychiatric medications (7.89%), analgesics (6%) and antibiotics (4.24%). Other medications accounted for the remaining 27.69% of the cases. We had no fatalities and the hospital admission rate was only 26.1%. Data were also examined for each year of the study period. *Conclusion:* In our study intoxications accounted for a small percentage of total admissions with figures not differing from the literature<sup>2</sup> with a better outcome than reported.<sup>3</sup> A large group of patients have unintentional iatrogenic poisoning. Alcohol consumption related intoxications are frequent as well. *References:* 1. Petridou ET, Dikaloti SK, Dessypris N, et al. The evolution of unintentional injury mortality among elderly in Europe. *J Aging Health* 2008; 20:159–82. 2. Yang CC. Acute poisoning in the elderly: an increasingly recognized but still overlooked problem. *J Chin Med Assoc* 2010; 73:183–5. 3. Mühlberg W, Becher K, Heppner HJ, et al. Acute poisoning in old and very old patients: a longitudinal retrospective study of 5883 patients in a toxicological intensive care unit. *Z Gerontol Geriatr* 2005; 38:182–9.

#### 217. Overdose of Pharmaceuticals for Alzheimer's Disease in Adults: A 3-Year Follow-up

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*Objective:* In Sweden, the first choice of pharmaceuticals for Alzheimer's disease is donepezil, rivastigmine, or galantamine. They all act as acetylcholinesterase inhibitors. There is limited information regarding accidental overdoses of these drugs among elderly patients. To clarify the risks, a follow-up study has been performed at the Swedish Poisons Information Centre. *Methods:* Inquiries from hospitals and the public regarding acute overdoses of pharmaceuticals for Alzheimer's disease among adults were recorded at the Swedish Poisons Information Centre. Hospital case records were collected and follow-up phone calls were performed. All cases with incomplete information, interfering co-ingestions or routes of administration other than oral were excluded. *Results:* Between March 2008 and March 2011, 166 cases of overdose of pharmaceuticals for Alzheimer's disease in adults were recorded. The majority of the inquiries came from the public (73%). A total of 53 cases (37 from the public and 16 from hospitals) were finally included. Forty-three people (81%) had taken a double or triple dose or another family member's medicine accidentally, nine had ingested a four to seven day dose unintentionally, and a single case concerned a suicidal attempt. Symptoms developed in 37 cases (70%), mainly of gastrointestinal nature (64%). Other mild symptoms reported included dizziness (17%), tiredness (15%), perspiration (11%), and headache (9%). More pronounced symptoms were observed in five hospitalized patients. Three patients developed cholinergic symptoms such as moderate respiratory insufficiency, frequent fasciculations, and sinus bradycardia. One patient had a short episode of unconsciousness followed by a short convulsion, and one displayed a prolonged QTc-interval after repeated vomiting. There was no fatality. The antidote, atropine, was used successfully for bradycardia in the only patient with intended self-poisoning. *Conclusion:* Patients with Alzheimer's disease constitute a difficult group to follow-up. Accidental overdoses of

donepezil, rivastigmine, and galantamine generated no or minor symptoms in most cases, and observation at home seems sufficient for most patients. However, there is still a possibility that hospitalization may be required in some patients, even after only small accidental overdoses of Alzheimer medications.

**218. Early Diagnosis and Timely Management are Crucial in the Prevention of Serious Bleeding in Patients with Superwarfarin Poisoning: Experience of the Poison Treatment Centre in Hong Kong**

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**Objective:** Superwarfarin poisoning can cause severe prolonged coagulopathy and fatal bleeding. We reviewed the clinical presentations and management of superwarfarin poisoning at the Prince of Wales Hospital Poison Treatment Centre (PWHPTC), a tertiary referral centre for poisoning management in Hong Kong. **Case series:** From June 2006 to October 2011, eight patients (median age 41 years, range: 18–90) with superwarfarin poisoning were referred to PWHPTC for management. Six patients ingested superwarfarins (bromadiolone = 5, brodifacoum = 1) for suicidal attempt. Of the five patients who presented within 24 hours of ingestion, three required vitamin K1 to correct their coagulopathy and none of them had bleeding. One patient presented with gross haematuria and vaginal bleeding 11 days after ingestion of 5 bottles of bromadiolone. INR and haemoglobin at presentation were > 5.0 and 5.9 g/dL, respectively. Two patients did not report ingestion of superwarfarin. Their diagnoses were delayed with severe bleeding symptoms. One patient was an 18-year-old lady who presented with abdominal pain to a surgical department. She had gross haematuria, menorrhagia and gum bleeding. Ultrasound examination showed evidence of haemoperitoneum. Haemoglobin was 11.5 g/dL and INR was > 5.0 with reduced factors II, VII, IX, X. She was treated with fresh frozen plasma (FFP) transfusion and vitamin K1 10 mg daily. She presented again two weeks later with persistent menorrhagia, anaemic symptoms and headache. Haemoglobin dropped to 4.8 g/dL and INR was > 5.0 again. Computed tomography showed intracranial haemorrhage. Serum assay confirmed the presence of brodifacoum. A 72 year-old man presented with gross haematuria to the Emergency Department and was treated as urinary tract infection with antibiotics. He presented again 4 days later with persistent haematuria. INR was > 5.0 with reduced factors II, IX and X. He did not respond to standard dose vitamin K1 and serum assay confirmed the presence of bromadiolone. The source was uncertain and a criminal act was suspected. Both patients responded to FFP transfusion and prolonged treatment with high dose vitamin K1. **Conclusion:** Clinicians must have a high index of suspicion when patients have unexplained prolonged PT/INR and bleeding in the absence of warfarin therapy. Early diagnosis and timely management are critical in the prevention of serious bleeding.

**219. Standardised Proforma Improves Risk Assessment and Overall Risk Stratification by Emergency Medicine Doctors Managing Paracetamol Poisoning**

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**Objective:** Physicians managing paracetamol (acetaminophen) poisoning in the UK currently undertake a process of 'risk stratification' to determine if an individual is at higher risk of paracetamol-related hepatotoxicity. A number of factors have been reported to be associated with increased risk, through reduction in intra-hepatic glutathione concentrations (e.g. eating disorders, HIV infection) or cytochrome P450 isoenzyme induction (e.g. chronic ethanol excess, use of enzyme inducing drugs). Inappropriate risk stratification can lead to harmful or potentially fatal under or over treatment. We introduced a hospital proforma to improve documentation and interpretation of risk factors associated with paracetamol-related hepatotoxicity; we describe here the effects of implementation of this proforma. **Methods:** We undertook a retrospective review of all patients presenting with paracetamol poisoning to our large inner-city Emergency Department, between 1st January 2010 and 31st December 2011. Data was collected on the documentation of risk factors associated with reported increased risk of paracetamol-related hepatotoxicity, the presence of the local hospital proforma and treatment outcomes. Cases with recording of at least one high risk factor, were deemed to have adequate documentation (since only one factor is required to make an individual 'high risk'); those where the documentation in relation to risk factors was determined to be insufficient to undertake a risk assessment, were deemed to have inadequate documentation. **Results:** Of the 249 presentations with paracetamol poisoning, only 59 (23.7%) had full documentation of all the risk factors associated with an increased risk of paracetamol-related hepatotoxicity required to make a complete risk assessment. Fifty-six (94.9%) of these had the local hospital proforma included in the notes and the remaining 3 (5.1%) did not. A local hospital proforma was more likely to be included in the ED notes in those with adequate documentation, 78 out of 120 (65%) compared to those with inadequate documentation, 16 out of 129 (12.4%) (chi-squared  $p < 0.001$ ). **Conclusion:** The use of our hospital proforma significantly increased the likelihood of documentation of the risk factors which increase risk for hepatotoxicity following paracetamol poisoning. Further work is needed to determine whether these results are repeatable in other centres.

**220. Hemorrhagic Complications in Patients Using Dabigatran**

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**Objective:** Dabigatran is an oral direct thrombin inhibitor approved for anticoagulation in non-valvular atrial fibrillation (AF). Despite decreased rates of thromboembolism in select patients, bleeding remains a therapeutic dilemma due to lack of antidotal therapy. We report four cases of severe hemorrhage with dabigatran use. **Case series:** We proactively collected all cases of dabigatran-related bleeding reported to the poison control center (PCC) and yielded four cases occurring between August and September 2011. Case 1. An 80 year-old man on dabigatran for AF was asymptomatic and had a non-focal neurological examination after falling and hitting his head. A CT showed a frontal subdural hematoma. He was discharged after serial imaging showed no progression. Case 2. A 73 year-old woman on aspirin and dabigatran for AF and anti-phospholipid syndrome

required an emergent median sternotomy for cardiac tamponade one week after an MI. She survived but required 8 units of fresh frozen plasma (FFP), 8 units of packed red blood cells (PRBCs), 2 units of platelets, and one unit of cryoprecipitate. Case 3: An 86 year-old man with chronic kidney disease (CrCl 31 mL/min), thrombocytopenia, and AF on dabigatran developed multiple episodes of rectal bleeding. He required transfusion with one unit of PRBCs, 2 units of FFP, and 2 units of platelets. Case 4. A 79 year-old man with a history of cardiac disease on aspirin, clopidogrel, and dabigatran developed rectal bleeding, epistaxis, and angina. He presented to the ED with a blood pressure of 64/47 mmHg. He rapidly deteriorated and despite resuscitative efforts, including massive transfusion, desmopressin, and 3000 units of prothrombin complex concentrate, he exsanguinated and died. **Conclusion:** While clinical trials demonstrated efficacy in preventing thromboembolic stroke, the absence of a definitive antidote raises concern for irreversible bleeding and death. Currently, dabigatran's only listed contraindications include active pathological bleeding and a history of serious dabigatran hypersensitivity reaction. Widespread use of dabigatran may yield severe hemorrhage rates higher than those observed in controlled trials. Concomitant bleeding diathesis, platelet disorder, simultaneous anticoagulation with antiplatelet agents, advanced age, renal insufficiency, and fall risk increase the likelihood of bleeding and should be considered as absolute or relative contraindications.

**221. Analysis of Discharge Notes of Acutely Poisoned Patients Focusing on Background History**

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**Objective:** Approximately 12,000 patients are discharged from somatic hospitals each year with ICD-10 codes of acute poisonings.<sup>1</sup> The national hospital statistics give few details concerning these cases.<sup>2</sup> We wanted to characterise acute poisonings treated in Norwegian somatic hospitals in 2008 with regard to the background history of the poisoned patients. **Methods:** We asked somatic hospitals to submit anonymous discharge notes from patients treated for acute poisonings in 2008. Data from the received notes were standardized, plotted in an Excel sheet and analysed. We registered several variables, including the presence of psychological problems, previous episodes of poisoning and history of alcohol or drug abuse. **Results:** 2301 discharge notes filled the inclusion criteria. The sex distribution showed a slight overweight of women (51.3%) compared to men (47.5%). Many of the discharge notes described previous patient histories; 43.6% of the patients had known psychological disease; 29.3% had experienced previous poisonings; and 30.8% had a history of alcohol or drug abuse. Several of the patients had multiple of these factors present. We registered 666 women and 321 men with known psychological disease, 419 women and 252 men with previous poisoning, and 233 women and 471 men with a history of drug abuse. In 73.4% of the patients the poisonings were considered to be related to self harm/suicidal intent or drug abuse. **Conclusion:** The majority of the patients (66.4%) had a background history with at least one of the factors registered, and several had more than one. A marked sex difference was seen, with psychological problems more common among women, and abuse problems more common among men. The data have to be interpreted with caution because of weaknesses in the study design. But this

kind of analysis gives relatively easy access to data not available from hospital statistics, confirming the often complex situation of this patient group. *References:* 1. Yearly reports to Poisons Information Department, Directorate of Health, from Norwegian Patient Register. 2. Lilleeng GH, Berg KJ, Gjertsen F, et al. [Acute poisonings in Norway 1999–2004. Morbidity and mortality]. [Article in Norwegian] *Tidsskr Nor Lægeforen* 2007; 127:1023–7.

## 222. Single Acute Warfarin Overdose Causing Significant Elevation in INR

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*Objective:* To describe a case of a significant rise in INR that resulted from a single acute ingestion of warfarin. *Case report:* A 27 year-old female presented to the emergency department one hour after ingesting 60 tablets of her roommate's warfarin and an unknown quantity of oxycodone/acetaminophen, ibuprofen, naproxen, and nortriptyline in a suicide attempt. Her past medical history was significant for nonalcoholic steatohepatitis and gastroesophageal reflux disease. Her vital signs were: blood pressure 141/91 mmHg, pulse 112/minute, respiratory rate 10/minute, temperature 36.6° Celsius, pulse oximetry 97% on 2L oxygen via nasal cannula. Her examination was significant for sedation, miosis, tachycardia, and hypoactive bowel sounds. An electrocardiogram showed normal QRS and QTc intervals. Her laboratory studies were significant for an INR of 1.1, 4-hour acetaminophen level of 45 micrograms/mL, AST 45 U/L, and ALT 75 U/L, both of which were lower than her baseline. The patient received prophylactic phytonadione 10 mg subcutaneously 8 hours post ingestion. Twenty-six hours after ingestion her INR rose to 2.7, and peaked at 5.1 at 51 hours post ingestion. At 53 hours post ingestion she received phytonadione 10 mg orally. An INR at 66 hours post ingestion was 2.1 and she received another dose of phytonadione 10 mg orally. Her INR remained mildly elevated to 1.5 at 7 days post ingestion. The next available INR one month after ingestion was 1.0. She had an uneventful hospital course and did not develop any abnormal bleeding. *Conclusion:* Bleeding risk due to oral anticoagulants increases exponentially with an INR greater than 5.0.<sup>1</sup> It is generally accepted that an acute overdose in a warfarin-naïve patient will not result in any significant elevation of the INR, and there are no case reports of such a rise in the medical literature. This patient developed a significant rise in INR despite prophylactic vitamin K therapy. Physicians should be aware that there is the potential for a clinically significant rise in INR after an acute, massive warfarin ingestion, especially in the setting of co-ingestants that cause delayed gut motility (opiate and anticholinergic). *Reference:* 1. Baglin T. Management of warfarin (coumarin) overdose. *Blood Rev* 1998; 12:91–8.

## 223. Attitude of Lone Private Medical Practitioners towards Poisoning Cases

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*Objective:* To find out the attitude of lone private medical practitioners (MPs) towards poisoning cases, and to

elicit their reasons and suggestions. *Methods:* A total of 150 lone MPs practising in rural areas were interviewed using a pre-tested anonymous questionnaire with reference to objectives. The data were classified into attitude, reasons for refusal and suggestions, and analysed statistically. *Results:* There were 48 females and 102 males. All female and 88 male MPs refused to take up poison cases, as they were not willing to face the emotions of the patients and care givers, spend time with these cases and handle medico-legal procedures. Only 14 lone male MPs took up poison cases and treated them, if uncomplicated, and did the needful to serious cases and referred them to the nearest Government, or private multi-speciality hospital. They got special recognition in the community and economic rewards as well. Their limitations were lack of technical facilities and supportive staff. Also, they would have liked to know more about treatment of complex poisons. *Conclusion:* Professional bodies should organise educational programmes on toxicology and administrative authorities should ease the procedures so that lone MPs have confidence to do the needful in poisoning cases during the golden hours and refer in good time if required. *References:* 1. Legal Duties of a Medical Practitioner in Dealing with Poisoning Cases <http://medicolegalhelpline.blogspot.com/2008/06/legal-duties-of-medical-practitioner-in.html> [accessed 13 Dec 2011]. 2. Consumer Protection Act and Medical Profession - Doctor - Patient Relationship [http://www.medindia.net/indian\\_health\\_act/consumer\\_protection\\_act\\_and\\_medical\\_profession\\_doctor\\_patient\\_relation-ship.htm](http://www.medindia.net/indian_health_act/consumer_protection_act_and_medical_profession_doctor_patient_relationship.htm) [accessed 13 Dec 2011].

## 224. Pediatric Ergot Alkaloid Exposures: A 12 Year Retrospective Study of Cases Reported to the California Poison Control System

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*Objective:* Pediatric ergot alkaloid exposures, although rare, have the potential to cause serious effects such as peripheral vasospasm and ischemia. Current poison control center and emergency department guidelines recommend 24-hour admission for all pediatric ergot alkaloid exposures. The goal of this study was to describe the outcomes from unintentional ergot-containing drug (or product) exposures in children and to identify the need for hospitalization in these patients. *Methods:* We performed a retrospective review of cases reported to the California Poison Control System (CPCS) from Jan. 1, 1997 – Dec. 31, 2008. Inclusion criteria: patients aged 6 and under with exposure to an ergot alkaloid-containing product in California. *Results:* A total of 374 cases were identified and 353 met inclusion criteria. The mean age was 26 months with > 99% oral route of exposure. The most frequent clinical effect was gastrointestinal distress (16%), followed by lethargy (5%). Two critically ill cases were identified, both with complete recovery. The first was a 2 yo M who presented with vomiting, lethargy, hypoxia and cool extremities after ingesting an unknown quantity of methylergonovine. Within 15 minutes of receiving IV fluids, supplemental O<sub>2</sub> and warm blankets he appeared better. The second case was a neonate with accidental intramuscular injection of methylergonovine 0.2 mg who developed respiratory depression and hypoxia, and quickly improved with supplemental facemask O<sub>2</sub>. For symptomatic patients, all symptoms were there at time of initial presentation. Sixty-two per cent of all patients were treated in the hospital setting. The median length of hospital stay was 4 hrs, ranging from 1–36 hrs. Ergot

exposures had a similar number of serious outcomes to other pediatric poisonings reported to the CPCS during the study period (Odds ratio [OR], 0.98; 95% confidence interval [CI], 0.25–3.95) but were associated with a significantly higher number of hospitalizations (OR 13.8; 95% CI, 11.1–17.1). *Conclusion:* Pediatric ergot alkaloid exposures were associated with few transient adverse effects but multiple hospitalizations. Current poison control send-in protocols and emergency department (ED) guidelines should encourage home management and short ED stays as opposed to lengthy critical care bed admissions.

## 225. Mercury – Kinetics in a Case of Mercury(II) Chloride Intoxication, Role of DMPS and Extracorporeal Regional Complexing Haemodialysis

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*Objective:* In cases of mercury (Hg) poisoning conventional haemodialysis (HD) with and without systemic chelator therapy is believed to remove only minute amounts of Hg. Here we report a case treated with DMPS and Extracorporeal Regional Complexing Haemodialysis (ERCH), which removed reasonable amounts of Hg by HD and shortened its half-life in blood. *Case report:* A 66 y, 80 kg male took in a suicide attempt 20 g mercury(II) chloride dissolved in 500 mL water, which resulted in instantaneous vomiting. He was carried to the hospital with hemorrhagic gastroenteritis 5 hours later (h 5). The physical examination was unremarkable except for some abdominal tenderness. The emesis and hemorrhagic diarrhoea resolved within the next hours. He had proteinuria and became anuric 16 h after poisoning (h 16). Chelation therapy with DMPS commenced 1 h after arrival: bolus 500 mg IV followed by continuous infusion of 2.5 g/day. HD (Fresenius Genius, F60) started at h 20. The next day DMPS was reduced to 1.5 g/day. Beginning with day 3 ERCH started: extracorporeal infusion of DMPS 100 mg/h into the “arterial” dialysis line. Hg concentrations of blood, serum, dialysate were determined by cold-vapor atomic absorption spectrometry (CV-AAS, ZEE nit 650 spectrometer with a HS 60 amalgamation unit, Analytik Jena). *Results:* Hg in blood at 5 h was 5.3 mg/L, in serum 5.4 mg/L; serum/corpuscular distribution (scd) 1:1.13. After 500 mg DMPS bolus: Hg blood: 5.5 mg/L, Hg serum: 8.0 mg/L, scd: 1:3.28. First HD removed 16.4 mg Hg, second HD 18 mg, third HD (DMPS IV 1.5 g/d) 12 mg. First ERCH removed 20.4 mg, second ERCH 17.3 mg. Blood Hg peaked at 33 h 6 mg/L. Hg in blood then declined with half-time 39 h (r<sup>2</sup> = 0.96) until h 120 (1.26 mg/L). *Conclusion:* A bolus of 500 mg DMPS IV caused a profound shift of Hg in blood from corpuscular to serum. With DMPS IV and via ERCH noteworthy amounts of Hg can be removed by HD. With these measures the half life of Hg in blood is shorter than known from literature (226 – 552 h).

## 226. How Many Poisoned Patients Transported by Emergency Medical Services Actually Require Hospital Treatment?

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**Objective:** Every year in the USA, emergency medical services (EMS) providers respond to thousands of calls for toxic exposures. However, these emergency providers have limited training in toxicology. Previous studies have demonstrated that EMS providers may effectively use poison centers (PCs) to determine those patients who do not require transportation to a hospital emergency department (ED). Our goal was to retrospectively determine the number of transported poisoned patients who did and who did not require treatment at one hospital. **Methods:** This was a retrospective review of PC charts of calls from Jan 2010 to Dec 2010. Inclusion criteria were (1) toxic exposure, (2) patient transported by EMS to one large teaching hospital, and (3) there was a call to a PC from a staff member at that hospital after the patient arrived. A patient was determined to have required treatment if any medical treatment (including activated charcoal) was administered in the ED or the patient was admitted to the hospital for medical or psychiatric treatment. **Results:** There were 193 PC charts that met the inclusion criteria. The patients' ages ranged from 1 month to 69 years old. There were over 50 different substance exposures, and 53% were intentional. Over half (50.8%) were admitted, 41.5% were discharged home from the ED, and 7.8% left against medical advice or disposition was unknown. Of those admitted to the hospital, 39.8% were admitted to psychiatry, 36.7% went to the intensive care unit (ICU), and 23.5% went to internal medicine. There was one death. Of the 80 discharged home, 14 received some ED treatment. Therefore, 66 (34.1%) did not appear to require transportation to the hospital. **Conclusion:** This is the first study of the disposition of poisoned patients transported to an ED by EMS providers. This small study reveals that over half are admitted to the hospital (many to the ICU). However, about one-third of all transported poisoned patients may not require transportation if a PC had been utilized at the scene. If some of these patients could remain at the scene with PC follow-up, this could decrease both pre-hospital and hospital resources.

### 227. Epidemiology of Acute Poisoning in Nis, Serbia

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**Objective:** Enough attention has not been dedicated to prevention of acute poisoning, and the relatively rarer accidental and criminal poisoning. Since the clinical toxicologist is familiar with all aspects of acute poisoning, from circumstances of poisoning to outcome, s/he should also be competent to consider the possibilities for prevention of acute poisoning. **Methods:** The purpose of this paper is to analyze acute poisonings, clinically treated and to define valid elements for proposals for prevention. The following were analyzed: the manner and circumstances of poisoning, neuropsychiatric disorders (NPS), other reasons for risk of poisoning and suicide, recurrence of poisoning, family history of suicide or severe neuropsychiatric disease. **Results:** Last year 1192 poisoned patients were examined at the clinic. The intoxications involved were: alcohol 386 (32%), pesticides 153 (13%), corrosives 184 (16%), heroin 112 (9%), drugs, 293 (25%) and others 64 (5%). Of the total intoxications, 723 (60%) were women and 469 men (40%). A high proportion of intoxications were in young people aged from 20 to 30 years and in patients over 60 years. The majority of cases involved intentional

ingestion of poisons, and only 5% of the cases involved accidental poisoning. In 98% of acute poisonings, drugs or toxic substances were located close at hand or in the immediate surroundings of the home environment. Of patients poisoned by drugs, 81% have been poisoned by the drug which was normally used in therapy. In 95% of those poisoned with chemicals they were taken from the immediate vicinity of the home environment. Of 21% of neuropsychiatric patients, 70% were not adequately treated, nor regularly monitored. There were 10% with recurrent intoxications and 45% with a family history of suicide or NPS disease. **Conclusion:** There is no need to hold large quantities of drugs in the household pharmacy, and toxic chemical substances should be kept well secured. This is especially true for families where there are suicidal, NPS patients, or chronic alcoholics. Precautions should be taken where there are younger people, emotionally unstable, with adolescent crises or who have made verbal statements about suicide, and the elderly with handicapped vision or psycho-organic disabilities.

### 228. Opioid Receptor Polymorphism Associated with Clinical Severity in a Drug Overdose Population

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**Objective:** Genetic variations in the mu-opioid receptor gene (OPRM1) mediate individual differences in response to pain and opiate addiction. We studied whether the common A118G (rs1799971) mu-opioid receptor single nucleotide polymorphism (SNP) was associated with overdose severity in humans. In addition, the SNP responsible for alternative splicing of OPRM1 (rs2075572) was also examined. We assessed allele frequencies of the above SNPs and associations with clinical severity in patients presenting to the emergency department (ED) with acute drug overdose. **Methods:** In an observational cohort study at an urban teaching hospital, we evaluated consecutive adult ED patients presenting with suspected acute drug overdose over a 12 month period for whom discarded blood samples were available for analysis. Specimens were linked with clinical variables (demographics, urine toxicology screens, clinical outcomes) then de-identified prior to genetic SNP analysis. In-hospital severe outcomes were defined as either respiratory arrest (RA, defined by mechanical ventilation) or cardiac arrest (CA, defined by loss of pulse). Blinded Taqman genotyping (Applied Biosystems) of the SNPs were performed after standard DNA purification (Qiagen) and whole genome amplification (Qiagen REPLI-g). The PLINK 1.07 genetic association analysis program was used to verify SNP data quality, test for departure from Hardy-Weinberg equilibrium and test individual SNPs for statistical association. **Results:** We evaluated 178 patients (37% female, mean age 41.2) who overall suffered 13 RAs and 3 CAs (of whom 2 died). Urine toxicology was positive in 33%, of which there were positives for 32 benzodiazepines, 26 cocaine, 21 opiates, 13 methadone, and 6 barbiturates. All genotypes examined conformed to Hardy-Weinberg equilibrium. The 118G allele was associated with 2.5 fold increased odds of CA/RA (OR 2.5,  $p < 0.05$ ). The rs2075572 mutant allele was not associated with CA/RA. **Conclusion:** These data suggest that the 118G mutant allele of the OPRM1 gene is

associated with worse clinical severity in patients with acute drug overdose. The findings add to the growing body of evidence linking the A118G SNP with clinical outcome and raise the question as to whether the A118G SNP may be a potential target for personalized medical prescribing practices with regard to behavioral/physiologic overdose vulnerability.

### 229. The Impact of the Drug Overdose Epidemic on the Mortality of Persons with HIV/AIDS

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**Objective:** In the highly active anti-retroviral therapy (HAART) era, acquired immunodeficiency syndrome (AIDS)-related causes of death have declined, while non-AIDS-related causes, especially drug overdose and liver disease, have become a leading cause of death in persons with human immunodeficiency virus (HIV). Excess mortality among HIV-infected patients has been identified in those with substance use dependence.<sup>1</sup> Our aim was to review the recent literature regarding the impact of HIV/AIDS on the current drug overdose epidemic with respect to the HAART era (1997 onwards). **Methods:** This systematic review screened PubMed database using search terms (HIV, AIDS, HAART, overdose, hepatitis, nephropathy, opioid, acetaminophen, methadone) and included cohort studies with derived mortality rates while excluding individual case reports, commentaries, letters, and publications over 20 years old. The crude overdose mortality rate (COMR) for each study was used to calculate a pooled COMR for each region during the post-HAART era. Calculation of 95% confidence intervals (CI) for COMR used 5% alpha. **Results:** The COMR in HIV-infected persons was calculated for 17 cohort studies that analyzed cause of death in 22,414 total cases of HIV infected individuals who died from overdose in the United States, Canada, Puerto Rico, Europe, and Asia. The COMR worldwide during the pre-HAART era was 4.0% (CI 0.9–7.16) but this figure significantly increased to 17.5% (CI 12.4–22.7) during the post-HAART era. Factors that contributed to the rising COMR included: demographic factors, chronic pain, acetaminophen use, intravenous drug use, prescription drug addiction, HAART use, and end-organ disease (nephropathy, liver disease, neurocognitive disorder). **Conclusion:** In the HAART era, AIDS-related causes of death declined, while deaths due to overdose significantly increased in HIV patients. The rise in COMR was primarily attributable to pharmaceutical drugs for pain management. AIDS-related end-organ diseases may possibly impair metabolism and physiologic responses to drug overdose. Future research should focus on expanded COMR reporting, drug misuse, and prognostic markers. **Reference:** 1. DeLorenzo GN, Weisner C, Tsai AL, et al. Excess mortality among HIV-infected patients diagnosed with substance use dependence or abuse receiving care in a fully integrated medical care program. *Alcohol Clin Exp Res* 2011; 35:203–10.

### 230. When Do Emergency Physicians Consult a Poison Centre? A Multicentre Analysis of Influencing Factors

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**Objective:** Poisoning is an important cause for emergency department (ED) consultation. Reporting rates to poisons centres (PCs) by emergency physicians have been shown to vary between 26%–34%, and were as low as 4%–12% in lethal poisonings. Since the factors influencing the decision of emergency physicians to consult a PC have not been studied in detail, we aimed at identifying case-specific, circumstance-specific, and institutional factors influencing this decision. We also aimed at identifying a putative underreporting of certain types of poisoning. **Methods:** A multicentre retrospective consecutive review of all – acute and chronic – poison-related consultations and admissions to the ED of a primary care hospital and a large tertiary care teaching centre involving adults between January–December 2007. All consultations to the PC performed by the participating EDs during the study period were extracted from the PC database. Data were matched and analyzed by logistic regression and generalized linear mixed models. **Results:** 545 poisonings were treated in the participating hospitals during the study period (350 (64.2%) in the tertiary care centre, 195 (35.8%) in the primary care hospital). The PC was consulted in 62 (11.4%) cases. The following factors were found to have a significant influence on consulting the PC: gender (female vs male) (OR 2.99; 95% CI, 1.69–5.29;  $p < 0.001$ ), number of substances ingested ( $> 1$  vs 1) (OR 2.84; 95% CI, 1.65–4.9;  $p < 0.001$ ), and situation (accidental vs non-accidental) (OR 2.76; 95% CI, 1.05–7.25;  $p = 0.039$ ). Age, hospital size, and previous medical history did not show a significant influence. The PC was consulted significantly more on Monday and Tuesday than on Sunday (OR 4.1; 95% CI, 1.54–10.93;  $p = 0.005$  and 3.56; 95% CI, 1.32–9.59;  $p = 0.012$ , respectively), and significantly less during the night shift (24 p.m.–8 a.m.) (OR 0.32; 95% CI, 0.16–0.65;  $p = 0.002$ ). Furthermore, the PC was consulted significantly more when patients were admitted to ICUs (OR 5.81; 95% CI, 3.25–10.37;  $p < 0.001$ ). The opposite is true for drugs of abuse (including alcohol) vs medications (OR 0.006; 95% CI, 0.002–0.17;  $p < 0.001$ ). Asymptomatic and severe (PSS = 0 and PSS = 3, respectively) vs mild cases were associated with a more frequent consultation of the PC (OR 4.48; 95% CI, 1.78–11.26;  $p = 0.001$  and OR 2.76; 95% CI, 1.42–5.38;  $p = 0.003$ , respectively). **Conclusions:** We found a significant underreporting of poisonings to our PC. Moreover, we identified some factors that are highly correlated with consultation of the PC.

### 231. Role of P-Glycoprotein in Norbuprenorphine Transport at the Blood-Brain Barrier in Mice: Considerations for Buprenorphine Respiratory Toxicity

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**Objective:** Several deaths by asphyxia and acute poisonings were attributed to buprenorphine (BUP) in drug addicts. The exact role of the BUP active metabolite, norbuprenorphine (N-BUP), is still unknown. We previously reported that NBUP was a P-glycoprotein

(P-gp) substrate *in vitro*. We hypothesized that an alteration of the active P-gp-mediated NBUP efflux may result in increased BUP-related deleterious respiratory effects in mice. **Methods:** Study of BUP and N-BUP respiratory effects using plethysmography in FVB wild-type and P-gp knock-out (KO) mice; study of 3H-BUP and NBUP transport at the blood-brain barrier (BBB) using *in situ* brain perfusion; analysis of the effects of PSC833, a specific P-gp inhibitor; radioactivity counting (after 3H-BUP infusion) and measurement of NBUP concentrations using gas chromatography/mass spectrometry assay (after NBUP infusion) in samples obtained from brain perfusion and right cerebral hemisphere. **Results:** P-gp KO mice in comparison to wild-type mice presented a significant increase in respiratory depression following BUP and NBUP administration, with a significant increase in BUP-related expiratory time ( $p < 0.0001$ ) and NBUP-related inspiratory time ( $p < 0.0001$ ). Using an *in situ* cerebral perfusion, a significant reduction in NBUP ( $p < 0.001$ ) but not BUP transport was observed in the brain of KO mice in comparison to wild-type mice. Similarly, pre-administration of PSC833, a potent pharmacological P-gp inhibitor, resulted in a significant reduction of NBUP ( $p < 0.001$ ) but not BUP transport in mice brain. **Conclusion:** P-gp gene suppression was responsible for a significant increase of BUP-mediated respiratory effects in mice. Worsening of BUP-related respiratory effects was attributed to a reduction in NBUP efflux out of the brain at the BBB. Our results clearly support the possible role of P-gp in BUP-related toxicity in humans, which may be considered in cases of P-gp gene polymorphism or drug-drug interactions involving direct P-gp inhibition or competition with other P-gp substrates.

### 232. The Factors Having an Effect on Lower Cholinesterase Levels

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**Objective:** Measuring pseudocholinesterase (PChE) is a simple test to evaluate the severity of intoxication with organophosphate and carbamate insecticides, because they inhibit PChE, but PChE does not reflect the severity and mortality in several studies. The basal level of PChE in patients who attempt suicide with insecticides could be low, because they are exposed to insecticides for a long time as they are engaged in agriculture. This is part of the reason that PChE level does not reflect the severity. There is no research on the basal level of PChE in the normal population in South Korea. The authors investigated the characteristics of the residents of Jeju, Korea having a low PChE level. **Methods:** Residents of Jeju aged over 60 years were randomly enrolled. The level of PChE, demographic data, medical history, and occupation were investigated. Groups (higher level vs lower level) were divided on the basis of the median value of PChE. For comparison between the two groups, Mann-Whitney test, Pearson chi square or Fisher's exact test were used. Logistic regression was used to evaluate the factors having an effect on low PChE level. **Results:** Twenty-eight (7.9%) residents were engaged in agriculture, having used insecticide recently, out of a total of 353 residents. Sixteen (4.5%) had lower PChE levels out of normal range (5,400–13,200U/L), and the lower group had 177

residents. The age of the lower group was older, and the high-density lipoprotein (HDL) level was lower than those of the higher group. Older age and lower HDL levels had a risk of lower PChE in univariate logistic regression, but the only risk factor was age in multivariate logistic regression. **Conclusion:** There are many potential causes of lower PChE to be considered; genetics, chronic disease, hepatic failure, liver cirrhosis, malnutrition, tumor, infection, and pregnancy. The only risk factor in this study was age. It will be necessary to investigate genetic factors and other risk factors contributing to lower PChE level in those under 60 years in the future.

### 233. On-Site Therapy Monitoring of Nerve Agent Poisoning

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**Objective:** Poisoning with nerve agents is a permanent threat for military and civilian health care systems. A high number of victims suffering from respiratory insufficiency are matched by limited capacities for ventilatory support. As nicotinic receptors are responsible for neuromuscular transmission, maintenance or restoration of their function is decisive for survival. Reactivation of inhibited acetylcholinesterase (AChE) by oximes is regarded as a promising attempt. Initial successful reactivation indicated by clinical improvement can be antagonised when an organophosphate is persisting while the concentration of the oxime is decreasing.<sup>1</sup> Thus, an appropriate parameter for on-line and on-site monitoring of oxime effects appears necessary. As red-blood-cell (RBC)-AChE is an appropriate parameter to follow oxime effects, a portable test system (ChE check mobile<sup>2</sup>) was developed that is able to determine this parameter within 4 minutes on-site. Here, it was investigated whether oxime effectiveness can be monitored with the ChE check mobile in VX poisoning. **Methods:** Anaesthetised swine were poisoned percutaneously with lethal doses of VX and treated thereafter with the oxime HI 6. RBC-AChE activity was determined on-line repetitively from venous whole blood using the ChE check mobile. **Results:** VX administration resulted in the development of cholinergic crisis that was accompanied by a marked decrease of RBC-AChE activity. When HI 6 was administered, RBC-AChE activity increased but dropped down again, when the HI 6 concentration decreased. Repetitive administration of HI 6 was again correlated with an increase of RBC-AChE activity. AChE activity could be determined immediately on-site. **Conclusion:** The commercially available ChE check mobile (CE certified IVD product) can be used on-site for diagnosis of an exposure to organophosphorus compounds and to monitor oxime effectiveness. It appears mandatory to follow oxime effects during therapy to prevent premature discontinuation of life saving oxime therapy. Otherwise, initially appropriately treated patients may deteriorate later on, when the effective oxime concentration decreases while effective poison concentrations persist in the body. **References:** 1. Eyer F, Worek F, Eyer P, et al. Obidoxime in acute organophosphate poisoning: 1 - clinical effectiveness. Clin Toxicol (Phila) 2009; 47:798–806. 2. Worek F, Baumann N, Pfeiffer B, et al. Mobiler Cholinesterase-Schnelltest zur Felddiagnostik einer Organophosphatexposition im Vollblut. Wehrmed Mschr 2011; 55:81–3.

### 234. Predictors of Intermediate Syndrome Following Acute Chlorpyrifos Poisoning

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**Objective:** To determine possible biochemical predictors of intermediate syndrome (IMS) following acute chlorpyrifos poisoning. **Methods:** Fifty-nine acute symptomatic chlorpyrifos poisoned patients were assessed clinically and electrophysiologically to detect the development of IMS. Blood was collected on admission, 1, 4, 12 and 24 hours following admission. Red blood cell acetylcholinesterase (RBC AChE), serum butyrylcholinesterase (BuChE) and serum chlorpyrifos levels were assessed by modified Ellman method, Ellman method and reverse-phase high performance liquid chromatography respectively. Cumulative measures of RBC AChE inhibition, BuChE inhibition and serum OP level were calculated as area under the curve (AUC) over 24 hours. The predictive power of the above parameters for the development of IMS was determined using Receiver Operating Characteristic (ROC) curves. **Results:** Of the 59 patients, 30 developed IMS. Admission RBC AChE, serum BuChE and serum chlorpyrifos levels were available in 34, 55 and 55 patients respectively. 24h AUC of RBC AChE, serum BuChE and serum chlorpyrifos levels were available in 46, 47 and 43 patients respectively (Table 1).

**Table 1.** ROC analysis of admission and 24 hour AUC values of RBC AChE, serum BuChE and serum chlorpyrifos levels in predicting the development of intermediate spectrum disorder.

Parameter	AUC of ROC	
	curve	95% CI
Admission bloods		
RBC AChE	0.610	0.393–0.828
BuChE	0.651	0.445–0.858
Serum chlorpyrifos	0.763	0.590–0.936
24 hour AUC value		
RBC AChE	0.728	0.518–0.938
BuChE	0.687	0.472–0.903
Serum chlorpyrifos	0.761	0.609–0.914

**Conclusion:** Admission serum chlorpyrifos level and the surrogate measures of 24 hour serum chlorpyrifos and RBC AChE were the best indicators of prognosis. Measurement of serum chlorpyrifos level may not be feasible in clinical settings. These results also need to be validated in larger prospective studies. Until such data is available patients should be closely monitored clinically and electrophysiologically to detect the development of IMS and subsequent late respiratory failure in acute chlorpyrifos poisoning.

### 235. The Effects of Fresh Frozen Plasma or Albumin in the Treatment of Acute Organophosphate Poisoning: What is the Clinical Relevance?

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**Objective:** Besides standard treatment of organophosphate poisoning (OP) bioscavenger therapy has also been explored. The rationale behind the use of fresh frozen plasma (FFP) that is rich in butyrylcholinesterase (BuChE) is that it may serve to neutralize free toxin. In addition, it has been shown that albumin may also scavenge organophosphate by adsorption. The objective was to evaluate the effects of bioscavenger therapy on cholinesterase levels and clinical outcomes in patients with moderate or severe OP poisoning. **Methods:** A prospective study was performed at the National Poison Control Centre during the previous 10 months. Fourteen patients were included in the study: all of them received atropine; FFP (2 x 250 mL/bag on day 1 and Day 2) was given to 6, and albumin to 3 patients. The incidence of mechanical ventilation, intermediate syndrome and mortality rate were determined. Butyrylcholinesterase levels of FFP were 10,868 ± 1078.5 U/L. **Results:** FFP increased butyrylcholinesterase levels (from 998.1 ± 459.6 to 1439.0 ± 511.8) significantly (p < 0.05) (Man-Whitney test), whereas non significant increase in BuChE levels was recorded with albumin (from 764.0 ± 100.2 to 838.3 ± 130.5) and standard therapy (from 628.1 ± 628.8 to 723.2 ± 611.2). Mechanical ventilation in the group of patients with bioscavenger therapy and standard therapy was 0% and 33.3% respectively. There were no cases of intermediate syndrome and all the patients had favourable outcome, with faster clinical improvement in patients with FFP therapy. **Conclusion:** The administration of FFP increases butyrylcholinesterase levels, reduces the need for mechanical ventilation and improves clinical outcome in patients with acute organophosphate poisoning. Butyrylcholinesterase replacement treatment may be used as an alternative approach in patients with acute organophosphate poisoning especially when oximes are unavailable. **Reference:** 1. Guven M, Sungur M, Eser B, et al. The effects of fresh frozen plasma on cholinesterase levels and outcomes in patients with organophosphate poisoning. *J Toxicol Clin Toxicol* 2004; 42:617–23.

### 236. Acute Organophosphorus Poisoning in Humans: A Pharmacokinetic Model for Chlorpyrifos

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**Objective:** Organophosphorus (OP) pesticide poisoning is an important problem in South Asia; acute poisoning from OPs in Sri Lanka resulted in 853 deaths in 2007 with the incidence increasing.<sup>1</sup> Characterization of the dose-concentration-response relationship would be useful to understand the time-course of acute poisoning. However, accurate information on dose amount and time of ingestion is generally lacking. In this analysis we aimed to develop pharmacokinetic (PK) and pharmacokinetic/pharmacodynamic (PKPD) models of one OP, chlorpyrifos (CPF), in acute poisoning. **Methods:** A PK model for CPF and its metabolites was developed using NONMEM VII. The model was derived from acute poisoning data from patients (n = 72; 7 female, age 15–65 years, 2–8 samples per subject). The reported volumes ingested ranged from 10 to 350 mL. CPF, chlorpyrifos oxon (CPO) and cholinesterase (AChE and BChE) levels were measured. **Results:** A

2-compartment model for CPF with first order absorption kinetics and a one compartment disposition for the active metabolite CPO best described the data. Dose uncertainty was accounted for by allowing each individual's dose to deviate from the median dose of 57.5 mL using the reported volume intake as a covariate on the relative bioavailability parameter. For CHL absorption was fixed to 1.64 (hr), Cl was 0.9 (L/hr), Vd 7.39 (L), Vp 33.9 (L) and Q was 1.65. A proportional residual error was estimated to 37%. The estimated dose range was on average 30 mL less than reported. **Conclusion:** The validated PK model developed characterised the observed concentrations of 0.1 – 19 nM well with reasonable estimates of the dose range. The PD model is under development and will incorporate cholinesterase inhibition, an important biomarker, and survival data. We hope this model will help us to better understand acute and chronic chlorpyrifos poisoning toxicology, the relationship between dose and PD outcomes and potential treatment options. **Reference:** 1. Editor, AH. Statistics. Morbidity and mortality. Medical Statistics Unit, Sri Lanka. 2007; p 38.

### 237. Electrocardiographic Findings as a Prognostic Marker in Acute Aluminum Phosphide Intoxicated Cases

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**Objective:** Aluminum phosphide (AIP) poisoning has a high mortality due to cardiovascular involvement.<sup>1</sup> In this study we aimed to evaluate the electrocardiographic (ECG) findings in acute AIP poisoning. **Methods:** We evaluated 20 patients with acute AIP poisoning who were admitted to the Intensive Care Unit (ICU) in Lohman Hakim Hospital Poison Center over a period of 6 months. The age, sex, cause of ingestion, number of ingested AIP tablets, cardiac and ECG findings and related laboratory data were extracted from the patients' files. All data were analyzed with SPSS software. **Results:** The patient's mean age was 27 ± 8.7 years. The majority (60%) of the patients were male. The mortality rate was 40%. There was no significant difference in the mean age and sex between survival and non-survival groups. In all of the patients the cause of poisoning was suicidal intention. The mean ± SD systolic blood pressure in survival (100.4 ± 14.5 mmHg) and non-survival (86.1 ± 13.5 mmHg) groups was significantly different. Dysrhythmia was observed in 45% of cases. Seven patients showed atrial fibrillation and 2 cases had junctional rhythm. There was a significant difference due to cardiac rhythm between survival and non-survival groups. Elevation of ST segment was seen in 45% of cases. The mortality rate in the patients who had ST segment elevation was 66.7% and 18.2% in the patients who did not have ST segment elevation, which was statistically significant. In 35% of patients, the QTc interval was prolonged. Bundle branch block (BBB) was observed only in 20% of patients. In 45% of patients, serum cardiac troponin-T (TnT) qualitative assay was positive. In 80% and 20% of patients, creatine phosphokinase (CPK) levels and CPK to CPK-mb ratio were increased. The number

of positive results for serum cardiac TnT qualitative assay were significantly different between survival and non-survival groups; but there were no significant differences between these groups according to CPK levels and CPK to CPK-mb ratio. **Conclusion:** There was a significant correlation between ECG findings and TnT positive results with outcome in acute AIP poisoning. **Reference:** 1. Proudfoot AT. Aluminium and zinc phosphide poisoning. *Clin Toxicol (Phila)* 2009; 47:89–100.

### 238. Surveillance of Medication Errors in Italy

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**Objective:** The National Poison Control Centre (PCC) in Milan, in collaboration with the Italian National Institute of Health and the Italian Medicines Agency, has recently implemented a national surveillance system of medication errors (MEs) based on data provided by PCCs. Aim of the present contribution is to provide a preliminary characterization of MEs handled by the PCC in Milan in 2006–2008. **Methods:** Descriptive analysis of the case data. **Results:** In the period under study the PCC in Milan handled 13,756 cases of exposure due to ME, accounting for about 30% of all cases of those unintentionally exposed to medicinal products. The observed MEs were mainly caused by incorrect dose (42% of cases) and exchange of drugs (37%). About 20% of cases were aged less than 1 year, 30% 1–5 years, 12% 6–19 years, and 33% more than 19 years. Male and female individuals were equally distributed. Most of the cases (80%) were asymptomatic, however, at least one treatment was prescribed for 40% of them. Among patients suffering signs or symptoms possibly related to the exposure, 34% reported neurological, 29% gastrointestinal, 10% neuromuscular, and 9% cardiovascular effects. The most common categories of agents involved in MEs were: analgesics (18%), antimicrobials (13%), pharmaceuticals for topical use and sedative/hypnotic/antipsychotics (7%, respectively), and antihistamines (6%). The most frequently reported agents were: acetaminophen (analgesic), amoxicillin (antimicrobial), oxatomide (antihistamine), benzodiazepines (sedative/hypnotic/antipsychotic). **Conclusion:** Directive 2010/84/EU clarifies that pharmacovigilance of medicinal products should also include noxious and unintentional effects resulting from MEs. PCCs could provide a relevant contribution by identifying this kind of effect and monitoring the safe use of authorised medicinal products.

### 239. Meprobamate Poisoning: Assessment of Risk Reduction Measures through French Poison Centres Data

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**Objective:** Meprobamate has been marketed in France as an anxiolytic drug (meprobamate-Anx) and a hypnotic drug (meprobamate-Hyp). Acute meprobamate poisoning may be life-threatening. In order to reduce the frequency and severity of meprobamate self-poisoning cases, the French Health Products Safety Agency (Afsaps) limited in 2006 the indications, and in 2009 the size of packaging for meprobamate-Anx, but not for meprobamate-Hyp. To verify the effectiveness of these measures, Afsaps requested the National Coordination Committee for Toxicovigilance for an analysis of the cases recorded by the French poison and toxicovigilance centres (FPTCs). **Methods:** A retrospective study analyzed the cases of meprobamate exposure collected from 2000 to 2010 by the FPTCs. The severity was defined by the presence of convulsions, coma, collapse, arrhythmias, cardiac arrest, acute pulmonary edema, bradypnea/apnea, respiratory distress, or death. FPTC activity and sale data of these drugs were used for adjustment. **Results:** Of the 12,870 cases collected, 5975 were related to meprobamate-Anx (symptomatic 67.0%, severe 18.8%, with death 0.9%), 6341 to meprobamate-Hyp (69.2%, 23.2% and 1.4% respectively), 308 to both and 246 to unspecified origin. The annual change in the number of cases showed a decrease for meprobamate-Anx, but not for meprobamate-Hyp cases. This decrease persisted after adjustment to FPTCs' activity and was parallel to changes in sale figures (only meprobamate-Anx cases decreased). Regarding severe cases, the evolution showed a decrease in the number of cases associated with meprobamate-Anx from 2006, together with an increase of cases associated with meprobamate-Hyp. **Conclusion:** This study shows that regulatory decisions efficiently decreased the sales of meprobamate-Anx as well as the number and severity of meprobamate-Anx poisoning cases reported to the FPTCs. It is too early to assess the effect of packaging reduction (effective only since 2009). Concerning meprobamate-Hyp there were no regulation measures at the time of the study, and no reduction of sales or changes in the number of cases were observed. In contrast, an increase of severe cases was noted, which persisted after adjustments. This study justified *a posteriori* the interest in risk reduction measures. Afsaps recently decided on the withdrawal of meprobamate-containing drugs indicated as anxiolytic/hypnotic from the market.

### 240. Gastrointestinal Symptoms after Oral Ingestion of Cleaners and Cosmetic Products Containing Surfactant: Results from a Prospective Multicentre Study in Germany

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**Objective:** Cleaning and cosmetic products containing anionic and non-ionic surfactants are considered to be of low toxicity. Oral exposure generally causes limited gastrointestinal irritation. Most common symptoms are nausea, vomiting and diarrhoea. One objective of this study was to evaluate the frequency and severity of gastrointestinal symptoms. We previously reported the respiratory injuries.<sup>1</sup> **Methods:** Prospective analysis of acute exposures during a seven month period in 3 German poisons centres (PIC). A follow-up call was performed at least 48 h after confirmed ingestion of soaps, shampoos, bath additives, general purpose cleaners, laundry detergents or manual dishwashing detergents.

Follow up information was collected with a structured telephone-interview based on a detailed questionnaire. The interviews were conducted by trained PIC staff. **Results:** 605 patients were included: 540 children, 42 adults, 23 seniors. Two hundred and fifty-eight patients developed gastrointestinal symptoms (210 children, 30 adults, 18 elderly persons), most often nausea and/or vomiting (96), slight cough (45), foaming (44), choking (42), diarrhea (41). Angioedema-like swelling of tongue and/or lips (for up to 2 days) was reported in 4 seniors after chewing a bar of soap. It was associated with difficulties in swallowing in 2 cases. Dehydration with renal failure after diarrhea was reported in a 70 yo woman. A 67 yo woman developed a fibrinous oesophagitis from laundry detergents. Hoarseness was reported twice after drinking a general purpose cleaner, once with laryngitis and aphonia for several days. **Conclusion:** After ingestion of surfactant containing products, gastrointestinal symptoms occurred in nearly half of all patients. However, adults and seniors developed gastrointestinal effects more frequently than children (74% vs. 38% respectively). The unexpected angioedema-like symptoms reported here in the elderly after chewing a bar of soap might reflect a greater vulnerability of the elderly to the irritant effects of anionic and non-ionic surfactants. Caustic oesophageal lesions caused by liquid laundry detergents, similar to our case, had been reported only once before.<sup>2</sup> **References:** 1. Färber E, Wagner R, Prasa D, et al. Respiratory injuries after oral ingestion of cleaning and cosmetic products containing surfactants. First results from a prospective multicentre study in Germany. *Clin Toxicol* 2011; 49:249. 2. Mathieu-Nolf M, Deheul S, Nisse P. Liquid detergent capsules: A New Risk. *Clin Toxicol* 2007; 45:386.

### 241. High Doses of Trimebutine: A Risk of Severe Poisoning?

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**Objective:** Trimebutine is one of the most popular digestive anti-spasmodic drugs marketed in France. However, 3 cases of severe poisoning (with cardiac and/or neurological complications) were recently collected and one was published<sup>1</sup>. To check this signal, the French Health Products Safety Agency (Afsaps) and the National Coordination Committee for Toxicovigilance decided to retrospectively evaluate the cases of exposure notified to different networks. **Methods:** A retrospective study of cases reported from the first of January 1999 to the 31st of May 2011 to poison and toxicovigilance centres (PTCs), pharmacovigilance centres (PVCs), drug dependence centres (DDCs) and/or companies was performed. Severe poisoning cases were defined by the occurrence of at least one of the following signs or symptoms: shock, convulsions, bradycardia, arterial hypotension below 80 mmHg, arrhythmia, bradypnea/apnea, cardiac arrest. Causality was evaluated using the French toxicovigilance method. **Results:** 366 cases with

symptoms were reported to PTCs and 49 were severe. The sex ratio (F/M) was 1.2 and the median age 20. In most cases signs and symptoms could be explained by the associated agents. However, 12 cases with bradycardia and/or convulsions (leading to death in 3 cases) deserve discussion, because the associated drugs could not fully explain the symptoms. Once duplication and published cases were eliminated, data from other PVCs, DDCs and companies provided one additional case of bradycardia with conduction disorder. **Conclusion:** This national retrospective multicentre study corroborated the initial signal: severe neurologic and cardiac complications can follow trimebutine overdosage. Past pharmacological and toxicological experimental studies also confirm the possible occurrence of conduction disorders and neurological hyperexcitability, after administration of large amounts of trimebutine. However, many questions remain unanswered, concerning: toxic doses, the respective roles of the parent compound and metabolites, and the possible individual susceptibility factors. Supplementary toxicological studies are recommended but prescribers and emergency physicians should already be aware of these potential severe complications of trimebutine overdosage. **Reference:** 1. Gaillard N, Couvreur J, Carret V, et al. [A medicine not so harmless as it appears: about an emergency case of acute voluntary poisoning with trimebutine (Debridat®)]. [Article in French] *Ann Fr Anesth Réanim* 2011; 30:93.

#### 242. Prognostic Factors and Management of Scorpion Envenomation in Morocco: Multivariate Analysis of about 240 Cases

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**Objective:** To analyze the epidemiological profile and identify the clinical risk factors involved in deaths caused by scorpion envenomation. Scorpion envenomation constitutes a public health problem in Morocco because of the frequency, severity and socio-economic consequences that they generate. The province of Kelâa des Sraghna, surveyed for this study, is situated in a zone of high incidence and high lethality caused by scorpion stings in Morocco. **Methods:** A prospective study was carried out in this province from January to December 2007. The study was conducted in adult and pediatric resuscitation. The descriptive analysis focused on the sociodemographic parameters (age, sex, time post sting (TPP)), clinical and therapeutic features. We conducted univariate analysis to identify factors predicting death by scorpion envenomation. **Results:** Our study contains 20 cases of death among 240 hospitalization cases. The median age was 12 years ranging from 1 to 86 years. The sex ratio (M/F) was 1.25. Based on clinical evaluation 23.8% of patients were classified in class I, presenting local signs, 65% were in grade II having systemic effects and 11.3% in class III with life threatening symptoms. Statistical analysis of the data showed that fever (OR = 11.93), sweating (OR = 4.38), tachycardia (OR = 11.73), vomiting (OR = 4.07), cardiovascular distress (OR = 13.9), neurologic distress (OR = 12.7), respiratory distress (OR = 6.89) are clinical severity factors statistically associated with death and aggravate vital prognosis of hospitalized patients. **Conclusion:** Death from scorpion envenomation in the province of

El Kelâa des Sraghna remains high (8.3%), despite the efforts performed by the national health authorities; therefore, a clinical audit of deaths is needed to detect shortcomings to be remedied.

#### 243. Systemic Envenomations Induced by *Physalia physalis* Observed on the Atlantic French Coast during the Summer of 2011

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**Objective:** During the previous 4 years, the number of envenomations by Atlantic man-of-war, *Physalia physalis*, registered by the Bordeaux Poison Center (CAPTV 33) has dramatically increased. The aim of the study is to describe the clinical features of the patients envenomed by *Physalia physalis* on the Aquitaine coast during the summer of 2011 and to assess healthcare efficiency. This study was managed by the CAPTV 33 and the Regional office of the French Institute for Public Health Surveillance (InVS). **Methods:** A space-time analysis was conducted between June 1st and September 30th 2011. Lifeguards from 30 of coastal Aquitaine's cities must declare each case of *Physalia physalis* envenomation. A detailed healthcare protocol was given to each aid station at the beginning of the season. The CAPTV 33 provided medical support to lifeguards and hospital emergency departments during all the study period. Envenomation records were centralized and completed by CAPTV 33 and transmitted to the Regional office of InVS for an epidemiological surveillance. **Results:** Overall, 885 patients were reported, with a sex-ratio M/F of 1.5 and a median age of 13 years old (range: < 1–86). General symptoms were observed for 15% of reported cases. Respiratory distress, fainting, confusion, muscle pain with fasciculations were the most frequently reported severe general symptoms. The mean time of onset was 20 minutes and the general symptoms usually disappeared in less than 2 hours with symptomatic treatment. The severity of these general symptoms, assessed by the poisoning severity score (PSS), was: 7.7% PSS3, 6.6% of PSS2, PSS1 85.6%. No deaths were reported. The maximum hospitalization duration was 24 hours. **Conclusion:** This study confirms that man-of-war envenomations are becoming an emerging health phenomenon in the French Atlantic coast. Health surveillance must be reinforced during future summers to reduce morbidity. The healthcare protocol must include local symptomatic treatment and the development of general symptoms must require medical management. **Reference:** 1. Labadie M, Lambrot AL, Mangwa F, et al. Collective envenomation by *Physalia physalis* on the French Atlantic coast. *Clin Toxicol* 2010; 48:309.

#### 244. H1 and H2 Blockers Preventive Effects on Development of Opioid Induced Non Cardiac Pulmonary Edema

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**Objective:** Opioid overdose could induce non cardiac pulmonary edema (NCPE), which is highly fatal. Using venous occlusion plethysmography, we previously showed that combined histamine-1 and histamine-2 receptor blockade (H1H2B) inhibits morphine induced arteriolar vasodilatation, edema and itching in healthy volunteers. This was histamine related.<sup>1</sup> This study is designed to evaluate whether early treatment with H1H2B could prevent NCPE in heroin and methadone overdose subjects. **Methods:** 84 eligible admitted methadone and heroin overdose cases were recruited in an ethically approved (N/MUMS/1440) double blind randomized control trial (2010). In addition to routine treatments, subjects received [1] cimetidine and cetirizine or [2] placebo (42 patients each). **Results:** Age, gender, mean group severity score of poisoning and prior addiction were not significantly different in these two groups. Second chest X-rays with abnormal findings including bronchovascular pattern and diffused infiltration, were significantly less present in case group (P = 0.013). Intensive care unit admission was also less frequent in case group (P = 0.014). For cases undergoing mechanical ventilation at some stage (n = 20; 13 in control group) or who died (n = 4; 3 in control group), their differences did not reach significant levels. For those few cases that underwent echocardiography, cardiac pulmonary edema was ruled out. **Conclusion:** Early treatment with H1H2B could prevent NCPE in heroin and methadone overdose subjects. More powerful studies are needed to establish H1H2B causal effects on opioid overdose induced fatalities. **Reference:** 1. Afshari R, Maxwell SR, Webb DJ, et al. Morphine is an arteriolar vasodilator in man. *Br J Clin Pharmacol* 2009; 67:386–93.

#### 245. Airway Epithelium Contamination by Respiratory Irritants: In Vitro Study

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**Objective:** In opposition to atmospheric pollutants, corrosive and toxic gases deserve more studies on their airway toxicity. The objective of this work was to qualify and quantify cellular toxicity of hydrochloric acid, ammonia and acrolein on an airway epithelium model. **Methods:** A 3D *in vitro* model of the Human Airway Epithelium was used to assess the toxicity of three representative contaminants: an acidic corrosive (hydrochloric acid), an alkaline corrosive (ammonia) and an electrophilic toxic molecule (acrolein). Their toxicity was assessed from the measurement of trans-epithelial electric resistance (TEER), lactate dehydrogenase (LDH) activity in medium culture, cell viability as well as cilia beating frequency. **Results:** The epithelium is able to survive exposure to concentrations up to 25mM in both cases of corrosive agents (hydrochloric acid and ammonia). Toxicity of the two corrosive agents was shown to be extremely concentration-dependant, with a critical threshold beyond which the epithelium completely loses its barrier function in less than 10 minutes, without reversibility. Whereas the deleterious effect of the acid and the base are rather similar, acrolein was shown to have a much higher toxicity (concentration limit of resistance lower than 0.25 mM), which seems to be independent of the dose regarding the time-effect. Its effect was more delayed (approx. 120 minutes), and to some extent, the epithelium seems to be able to recover from the lesions at 0.5 mM but not at 1 mM. **Conclusion:** Measure of

TEER seems to be the earliest and the most accurate parameter to follow intensity and kinetics of airway epithelium lesions. The three contaminants chosen are present in fire smoke, as well as particulates and systemic toxins, and may exacerbate and worsen the injury due to systemic toxins in smoke inhalation sufferers after a critical threshold is reached. This observation strengthens the call for more aggressive research to develop a strategy of efficient pulmonary decontamination.

#### 246. An *In Vitro* Assessment of the Effect of Intravenous Lipid Emulsion on Total Drug Concentrations in Human Plasma Utilising Drugs Commonly Implicated in Cardiovascular System Poisoning

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**Background:** The most commonly suggested mechanism of action for lipid emulsion (ILE) in poisoning is that it acts as an intravascular 'lipid-sink', allowing lipophilic drugs to bind with lipid molecules, reducing free plasma-drug concentrations. Little data exist assessing the interaction of ILE with drugs of varying lipid solubility. **Objective:** To assess the *in vitro* effect of ILE on total drug concentrations in human plasma exposed to various drugs implicated in cardiovascular system (CVS) poisoning and relate the findings to octanol:water coefficients of the drugs tested (LogP(octanol)). **Methods:** Human plasma (1 mL samples) containing either amitriptyline, dothiepin, or clomipramine, verapamil or diltiazem, propranolol or atenolol, was incubated with 20% ILE (20, 100, 200 microlitres/mL) or equal volumes of phosphate-buffered saline (Control) in triplicate. Samples were centrifuged and the drug concentration in ILE-free plasma was assayed by GC/MS. Differences in drug concentrations between ILE and Control samples were expressed as percent-decrease ( $\pm$  95% CI) from Control. Unpaired t-test was used to compare drug concentrations between ILE samples and their respective Controls. **Results:** There were statistically significant decreases in ILE-treated plasma drug concentrations for the cyclic antidepressants and calcium channel-blockers. However, neither beta-blocker showed a significant decrease in drug concentrations at any ILE dose. Plasma drug concentrations fell more with increasing ILE concentration (See Table 1). **Conclusion:** A higher LogP(octanol) appears to correlate with *in vitro* reduction in plasma drug concentrations in the presence of ILE. Propranolol

and atenolol, with the lowest LogP(octanol), did not exhibit significant sequestration into ILE. This technique may be a simple way to screen drugs for their potential binding to ILE.

#### 247. Relation between Drug Lipophilicity and Effectiveness of Intravenous Fat Emulsion Treatment

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**Objective:** To assess the overall efficacy of intravenous fat emulsion (IVFE) treatment in animal studies and estimate the variation of efficacy, as well as the correlation between efficacy and lipophilicity of the target drugs to provide a better understanding for the application and limitations of this treatment principle. IVFE is used for the treatment of cardiotoxicity induced by lipophilic drugs. The evidence of its efficacy is primarily based on animal studies which, dependent on target drug and outcome measure, show varying results. **Methods:** Animal studies comparing the effect of IVFE with placebo, water, no treatment or an active comparator by means of improved hemodynamic parameters (BP or mean arterial pressure (MAP)) or lethal dose (LD50), survival time, survival rate or return of spontaneous circulation (ROSC) were categorized according to their endpoints into three groups; 1) studies with continuous endpoints dependent on time of assessment (BP and MAP assessed 15 minutes after IVFE), 2) studies with continuous endpoints independent of time of assessment (LD50 and survival time), and 3) studies with categorical endpoints (survival rate and ROSC). Separate meta-analyses were conducted for each group using standardized mean differences (SMD) for summary statistics of continuous and odds ratio (OR) for categorical endpoints. In addition, regression analyses for the relation between SMD and lipophilicity (logarithm of the ratio of the concentrations of the unionized solute in the solvents water and octanol (log P)) of target drugs were performed. **Results:** Eleven studies, including six different drugs were included in the analyses. Log P ranged from 0.5 to 5.2. IVFE significantly improved outcome of time dependent (group 1) and independent continuous parameters (group 2) (SMD 1.23 (95%CI 0.36, 2.09) and 1.24 (95%CI 0.65, 1.82) respectively) but failed to show significant improvement in group 3 (OR 8.19, 95%CI 0.32, 211). Drug lipophilicity was positively correlated to the SMD of time independent continuous outcomes ( $r = 0.69$ ,  $p = 0.10$ ) and the SMD of time dependent continuous outcomes ( $r = 0.75$ ,  $p = 0.03$ ). **Conclusion:** The efficacy of IVFE on the reversal of drug induced cardiotoxicity in animals is highly variable and dependent on the degree of drug lipophilicity.

#### 248. Analytical Tools for the Diagnosis of Acute Poisonings

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**Introduction:** Analytical tools are complementary methods in the acute poisoning diagnosis process. The evolution of chemical analytical techniques in recent decades has rendered theoretically possible the detection and quantification of nearly every possible poison involved in human intoxications. However, in daily practice the fact is that one only finds what one is looking for and, moreover, that it is impossible to have at one's disposal a complete array of analytical instruments, at every possible healthcare level. Thus, it is imperative to decide which tools are urgently needed, and this decision depends on the influence which analytical confirmation can have on therapeutic decisions. Analytical resources must be tailored to local epidemiological profiles, as it makes no sense to maintain analytical tools for virtually non-existent chemical substances in one's area, for economic and technical reasons. The application of the biomarker concept to the acute toxic field is meaningful and helpful but needs to be interpreted in light of toxicokinetic and clinical concepts. The presence of an exogenous substance in a biological sample demonstrates the exposure to this substance at some time prior to the obtaining of the sample, but does not establish an etiological or causal relationship with a clinical picture. Toxicokinetic factors determine the valid chronological interval for detection and the significance of quantification. The main clinical criteria for analytical usefulness are: 1st: The analytical data determine the therapeutics, which occurs in the indication for the use of some antidotes and/or elimination techniques; 2nd: It establishes the prognosis evaluation; and 3rd: It allows for etiological confirmation of the clinical diagnosis. **Methods:** To evaluate the efficiency of the different analytical methods in a practical situation, we have analysed data on the activity of the Unit of Clinical Toxicology, which is the leading Toxicology Laboratory for a region of 1,300,000 inhabitants in Spain. From more than 30,000 entries in our database over the last 20 years, we have reviewed the criteria for decisions on the implementation of instruments and the urgency of results for the top ten most involved substances, along with some of the less frequent but most dangerous substances. **Results:** Evaluated substances were: ethanol, benzodiazepines, cocaine, cannabis, antidepressants, amphetamines, opiates, neuroleptics, caustics, carbon monoxide (CO), paracetamol, methanol, paraquat, organophosphates, amatoxins and cyanide (HCN). **Discussion:** The laboratory can provide two kinds of data useful for the diagnosis of acute poisoning: direct and indirect biomarkers. Direct biomarkers of acute poisoning are the detection and quantification of toxic substances and/or metabolites in blood and urine. The type of instrument needed depends, obviously, on the chemical nature of the substance: metal compounds are analyzed by means of atomic absorption spectrophotometry. As for organic compounds, the main methods are currently molecular absorption spectrophotometry for colorimetric and immune-enzymatic (EMIT) techniques, and gas or liquid chromatographic techniques with different columns and detectors (GC/FID, GC/MS, HPLC and others). 1. The most accessible among these are the EMIT and colorimetric techniques, which can be installed in automatic analyzers, offering results in a few minutes. They provide semi-quantitative and quantitative information on many abused drugs and medications. Their sensitivity is high and their specificity varies for different

**Table 1.** Percentage fall ( $\pm$  95%CI) in drug concentration in human plasma (ratio: ILE/control).

Drug (concentration)	20% ILE 20 ml/L	20% ILE 100 ml/L	20% ILE 200 ml/L	LogP (octanol)
Amitriptyline (1 mg/L)	18% (9–27)*	42% (29–56)*	58% (57–60)*	4.94
Dothiepin (1 mg/L)	13% (–1–27)*	35% (21–49)*	54% (52–55)*	2.8
Clomipramine (1 mg/L)	0%	31% (25–36)*	58% (39–75)*	5.2
Verapamil (1.5 mg/L)	0%	36% (31–41)*	53% (49–56)*	2.41
Diltiazem (1.5 mg/L)	11% (–46–69)	24% (0.04–48)*	33% (10–56)*	2.79
Propranolol (2 mg/L)	4% (–19–28)	7% (–22–35)	11% (–0.1–22)	1.2
Atenolol (4 mg/L)	0%	0%	0%	0.23

\*Significant fall from matched control samples ( $p < 0.05$ ).

products. For most of the medications currently tracked by drug monitoring programs (e.g. digoxin, anti-epileptics...) they are highly accurate. For some types of substances their specificity is moderate, and does not allow for discrimination between different members of the same family (e.g. benzodiazepines or opiates). Their cost in terms of instruments, reagents and staff, is low. Serum ethanol can be measured by these analyzers by means of the enzymatic NAD-ADH technique, but it is important to remember that serum ethanol is about 0.3 g/L higher in serum than in blood, so for legal purposes it is imperative to analyze total blood by means of head space GC/FID. New legal and illegal drugs challenge this type of automated technique, due to the lack of specific reagents, and need to be detected through chromatographic methods. 2. CO-oximetry and Pulse Ox and CO-oximetry. The COoximeter has been accessible for Emergency Laboratories for the last few years, making the diagnosis of CO poisoning and methemoglobinemic agents much easier. An important and recent advance has been the portable COoximeter, which allows for quite accurate CO poisoning diagnosis prior to hospital arrival. 3. Chromatographic methods are highly sensitive and specific. Their cost in reagents is low, but the instruments and specialized staff required are very expensive. They could detect and quantify virtually any organic molecule, but these costs force them to be placed in highly-specialized laboratories that should act as centres of reference for a region, and should be able to provide an analytical result in a few hours. The same can apply to atomic spectrophotometric techniques for metallic compounds, although they are present in biochemical laboratories for the quantification of essential metals and can be adapted to the toxicology field. Indirect biomarkers are indispensable to evaluate the clinical status of the patient ( $O_2$  saturation, pH, bicarbonate, lactate, glucose, ions) but can also provide meaningful clues regarding exposure and effect (calculation of anion and osmolar gap, cholinesterase activity, coagulation status and enzymatic markers of hepatic, renal, myocardial or muscular damage). Most or all of them are currently accessible at the hospital's Emergency Laboratories. **Conclusion:** Several questions need to be answered in order to establish a decision with regards to the analytical tools to be implemented at each healthcare level: What could we do? What can we afford to do? What do we need to do? By combining epidemiological and clinical criteria, this decision can be adapted as a part of a realistic approach for different areas. **References:** 1. Flanagan RJ. The poisoned patient: the role of the laboratory. *Br J Biomed Sci* 1995; 52:202–13. 2. National Poisons Information Service, Association of Clinical Biochemists. Laboratory analyses for poisoned patients: joint position paper. *Ann Clin Biochem* 2002; 39:328–39. 3. Eldridge DL, Holstege CP. Utilizing the laboratory in the poisoned patient. *Clin Lab Med* 2006; 26:13–30, vii. 4. Rentsch KM. [Laboratory investigations in acute intoxications-what makes sense?] [Article in German]. *Ther Umsch* 2009; 66:365–71. 5. Rentsch KM. Laboratory diagnostics in acute poisoning: critical overview. *Clin Chem Lab Med* 2010; 48:1381–7.

#### 249. Container Fumigation and Health Disorders in Germany

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**Objective:** Health risks associated with the fumigation of containers have been increasingly discussed in recent years. Evaluation of data has shown that in the context

of the German physicians' reports on cases of poisoning under § 16e Chemicals Act, the BfR received spontaneous reports on 23 cases involving 1,2-dichloroethane and methyl bromide between 1990 and 2007. **Methods:** Alerted by this problem, the BfR initiated a survey among poisons centres (PCC) in Germany (nine centres), Switzerland, Austria and France in late December 2007. PCCs were asked whether they had received any enquiries regarding the fumigation of containers since the year 2000 and whether an increasing trend could be seen in the numbers of such enquiries. The active substances referred to in this survey included chloropicrin, 1,2-dichloroethane, methyl bromide and sulfurilyl difluoride. In addition, information was requested with regard to manifestations and degrees of severity of corresponding cases of poisoning. **Results:** The survey among the PCCs provided additional cases from Berlin, Erfurt, Freiburg and Zurich between 2003–2007. All the cases, including BfR reports, referred to 30 poisoning incidents that had affected a total of 71 persons. The substances incriminated were in the main part methyl bromide, only in some cases 1,2-dichloroethane, 1,2-dichloromethane, phosphine and unknown agents were indicated. One person had moderate, 65 persons had mild symptoms and signs, and in 5 persons no symptoms occurred. Symptoms reported included above all irritation of the mucous membranes of the upper respiratory tract and of the eyes, such as dryness of mouth, tickling throat, cough, lachrymation. Also headache, dizziness and malaise as well as skin rash and pruritus were frequently reported. **Conclusion:** In general, it has to be assumed that the frequency of cases of poisoning associated with fumigation of containers is highly underestimated in Germany. The BfR is investigating fumigation, held an Expert Meeting (<http://www.bfr.bund.de/cd/28565>) and is making efforts to inform the public in appropriate ways.

#### 250. Acute Intoxications by Herbal Blends Containing Synthetic Cannabinoids

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**Objective:** After the ban of the synthetic cannabinoids CP-47,497-C8 and JWH-018 several other compounds with agonistic activity on the CB1 receptor were identified in herbal blends.<sup>1</sup> We report about 35 emergency department (ED) patients with analytically verified consumption of such synthetic cannabinoids. **Case series:** Serum samples of 41 ED patients were analysed by LC-ESI-MS/MS after self reported consumption of synthetic cannabinoids, as described before.<sup>1</sup> The intake of these compounds was analytically confirmed in 35 patients (32 male, 3 female; median age 17.5 years). JWH-210 (31), JWH-122 (10), AM-2201 (7), JWH-081 (3), RCS-4 (2), JWH-203 (2) and JWH-018 (1) were identified. Most frequent clinical symptoms were tachycardia (74%), nausea/vomiting (66%), somnolence (57%), mydriasis (46%) and hypokalemia (40%). Less frequent symptoms were reduced or missing pupillary light reflex (20%), agitation (17%), vertigo (14%), paresthesia (11%), aphasia (6%), dysphasia (6%), generalized seizures (6%), myoclonia or muscle jerking (6%), hypopnoea with hypoxemia (3%) and massive aspiration with respiratory insufficiency (3%). Most symptoms ceased within hours, but aphasia lasted for more than one day. **Conclusion:** We found JWH-210 in most serum samples, while other synthetic cannabinoids were less frequently detected. The case series confirms a shift towards synthetic cannabinoids with greater affinity to the CB1 receptor (JWH-210 twentyfold above JWH-018). In contrast to former reports somnolence developed 3 times more frequently than agitation. Hypopnoea with hypoxemia and

aphasia have not been reported yet. Since most former published intoxication cases were due to JWH-018, these symptoms may be typical for the new synthetic cannabinoids with high CB1 receptor affinity. Six of 41 analysed serum samples were negative for cannabinoids. Analytical evidence and a thorough clinical examination is a prerequisite to better assessing the toxicity of these compounds. **Reference:** 1. Dresen S, Kneisel S, Weinmann W, et al. Development and validation of a liquid chromatography-tandem mass spectrometry method for the quantitation of synthetic cannabinoids of the aminoalkylindole type and methanandamide in serum and its application to forensic samples. *JMS* 2011; 46:163–71.

#### 251. Evolution of Blood Ethanol Concentrations at Traffic Controls. Validation of a Formula to Calculate the Imprecision of a Retrospective Extrapolation

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**Objective:** To verify the evolution of blood ethanol concentration (BAC) between two different moments at traffic controls for driving under influence (DUI). The admission of a blood sample taken some time after the moment to be evaluated and after the breath sample analysis as legal proof of DUI makes it important to know the pattern of the blood ethanol concentration between two times in real situations. **Methods:** We have analysed the BAC evolution in samples received at our laboratory coming from traffic controls over the last 20 years. The breath ethanol concentration was obtained by means of the standard evidential ethylometer currently used by the traffic police, while the BAC was measured with head space GC/FID. We show the relationship between the results of the BAC extrapolated from the roadside breath test (CO), and the BAC in the blood sample (Ct) taken some time later (t), and the evolution of BAC in relation to the time (t) elapsed between these two moments. We used the conversion factor (CF) admitted by law (2000 fold) and the conversion factor described as the median value in human experimental models (2100 fold) for the purpose of breath/blood extrapolation. **Results:** Number of cases 952. (CO) mean = 1.346 g/L (CF = 2000) and 1.413 g/L (CF = 2100). (Ct) mean = 1.268 g/L. t mean = 71.8 minutes (range 17–388). The evolution of BAC shows the following pattern: applying a CF = 2000, in 66.7% of the cases (Ct) < (CO), in 1.9% of the cases (Ct) = (CO) and in 31.4% of the cases (Ct) > (CO); applying a CF = 2100, only in 22.58% of the cases (Ct) > (CO). **Conclusion:** By using a linear regression model, plotting the variation of BAC and the time interval, and adjusting the difference of each piece of data with the predicted value following a normal distribution, we have developed a formula to predict, with a confidence interval of 99%, the range of values of a BAC at a given, previous time from the current BAC. The range of this estimation is very wide in a concentration and time-dependent function.

#### 252. Substance-Dependent Patients in a Methadone Maintenance Treatment Clinic in Northern Iran: A Descriptive Study

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**Objective:** Iran is one of the countries most affected by drug abuse. Around 2.8% of the population use opiates. Addiction to opioids poses serious problems for communities, families, and individuals. Methadone maintenance therapy (MMT) is a major intervention widely used as a replacement in the treatment of opium dependence in many countries, including Iran. The aim of this study was to characterise patients presenting to a MMT clinic in a referral hospital for drug addiction treatment. **Methods:** This cross-sectional descriptive study was performed over a one-year period from April 2009 to March 2010 and included all patients referred to the MMT clinic for drug dependence treatment in Zare Referral Hospital for psychiatric illness in the city of Sari, northern Iran. Data including demographic characteristics, types of drug dependence, previous history of addiction treatment, history of psychiatric illness, and other data were obtained prospectively using a questionnaire, face to face interview and patient's case note review. The study was approved by the local ethics committee. Collected anonymised data was analyzed using descriptive statistics. **Results:** Over a one year period 250 patients with mean age of  $39.5 \pm 11.3$  y presented to MMT clinic for opium addiction treatment, of whom 200 subjects provided the required information for the study. Most patients were married (78%) and from an urban area (71%). More than half of the cases had high school or higher education. Most patients abused multiple drugs simultaneously. More than 75% of patients had a previous history of drug dependence. Opium was the most common type of drug dependency (78%) followed by crack (40%) and crystal (31%). Less than half of the patients (43%) had a previous history of addiction treatment. Twenty-one per cent of cases had a family history of addiction. Two persons were HIV positive and one hepatitis C (HCV) positive. Depression (33.5%) and anxiety (31.5%) were the most common diagnosed psychiatric illnesses. **Conclusion:** The data from this study shows that opium is still the most common substance of abuse in Iran. Most of the affected people are young adults with high school education or higher indicating the importance of preventive strategy in society to avoid further psychosocial consequences.

### 253. Trends in Ephedrine, Pseudoephedrine and Methylamphetamine Poisoning Following Restriction of Over-the-Counter Availability of Ephedrine and Pseudoephedrine

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**Objective:** To evaluate whether restriction of UK sales of pseudoephedrine (PSE) and ephedrine (EPH) since 01/04/2008 led to reduced exposure to methamphetamine (MAM). Previous reports have suggested that these restrictions were associated with a drop in the wholesale purchases for PSE (24%) and EPH (8%) in the UK.<sup>1</sup> **Methods:** UK clinicians managing exposures to poisons usually access a clinical toxicology database (TOXBASE®) for management advice. In this study we use TOXBASE® accesses to product pages as a surrogate for potentially toxic exposures presenting to clinicians in the UK. Accesses by students and those from outside mainline UK were excluded. The number of monthly accesses to PSE, EPH and MAM between March 2005 and December 2010 were obtained, and mean monthly exposures for the two years pre-legislation compared with two years post-legislation. Changes in exposures to other sympathomimetics involved in chronic abuse (amphetamine, cocaine and MDMA) were obtained for comparison with MAM. **Results:** See Table 1.

**Table 1.** Comparison of monthly accesses to pseudoephedrine, ephedrine and methamphetamine on TOXBASE®, March 2005 – December 2010.

	Mean of pre-2008 monthly exposures	Mean of post-2008 monthly exposures	Change post-2008: Mean (95% CI)	% decrease	p-value
EPH	34.37	45.8	+11.42 (-19.60 to -3.23)	+33%	<0.01
PSE	52.42	28.96	-23.46 (16.49 to 30.43)	-45%	<0.001
MAM	22.71	7.17	-15.54 (10.83 to 20.25)	-68%	<0.001
Amphetamine	404.71	365.6	-39.1 (-1.4 to 79.6)	-10%	0.06
Cocaine	521.5	492.6	-28.9 (-10.2 to 68.0)	-6%	0.14
MDMA	655.7	307	-348.7 (302.3 to 395.0)	-53%	<0.001

**Conclusions:** There was a significant fall in accesses to PSE. EPH accesses increased significantly, perhaps because patients switched from PSE to mixed preparations containing low doses of EPH. There was a significant fall in MAM exposure which may be related to PSE restriction. The reasons for changes in MDMA are unclear. Further studies using clinical data are needed to confirm whether reduced accesses were associated with reduced sympathomimetic poisoning. **Reference:** 1. MHRA Public Assessment Report: Pseudoephedrine- and ephedrine-containing medicines: 2011 review of actions to manage the risk of misuse. August 2011 Accessed on 8/9/2011 from: <http://www.mhra.gov.uk/home/groups/pl-p/documents/web-siteresources/con126279.pdf>

### 254. Iranian Substance Abuse Warning Network: Pilot Results among Poisoned Patients

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**Objective:** The socio-medical phenomenon of drug abuse remains among the most critical issues facing our society today.<sup>1</sup> The Drug Abuse Warning Network (DAWN) is an important source of national and local information on substance abuse which is derived from drug screening tests on visits to hospital emergency departments and drug-abuse related deaths.<sup>2</sup> The present study reports the pilot results of DAWN in Loghman-Hakim center-Tehran, Iran. **Methods:** 16 substances were evaluated randomly using urine screening immunoassay kits among emergency poisoned patients in Loghman-Hakim center during 12 months. A trained physician collected hospital admission data through interview of patient/family using a self-made questionnaire. Descriptive analysis was used to analyze the data. **Results:** In total 1850 patients were chosen randomly to be interviewed and screened for drugs of abuse in the emergency department. Of these 1258 (68%) including 739 (58.7%) women agreed to enter the study. The mean age was  $28 \pm 11$  (range 12–88). In total 945 (75.1%) patients had deliberately poisoned themselves, while substance intoxication was the cause of admission in 194 (15.4%) patients. Opioids including tramadol (239; 27.5%), benzodiazepines (213; 16.9%), stimulants (46; 3.6%), ethanol (54; 4.3%), hallucinogens (8; 0.8%), barbiturates (7; 0.6%), solvents (1; 0.08%) were claimed to be used or abused in the past week. Morphine (249; 19.8%), methadone (157; 12.5%), buprenorphine (21; 1.7%), oxycodone (3; 0.2%), tramadol (127; 10.1%), propoxyphene (5; 0.4%), amphetamine (60; 4.8%), metamphetamene (100; 7.2%), cocaine (4; 0.3%),

MDMA (19; 1.5%), phencyclidine (25; 2.0%), ketamine (225; 17.9%), THC (25; 2.0%), barbiturate (18; 1.4%), benzodiazepine (486; 38.6%), ethanol (36; 2.9%) were positive in patients and the total number of abuse patients reached 798 (63.4%). A mean of two substances for each individual was achieved among test-positive patients. **Conclusion:** It seems that local antidrug efforts in Iran are not enough. Establishing a warning network to quantify the extent of the nation's drug problem, guiding resource allocation decisions, surveillance of local area drug trends, documentation of drug problems and trends, and providing a data source for academic research on drug abuse are our national priorities. **References:** 1. UNODC United Nations Office on Drugs and Crime. World Drug Report 2011. Available at: [http://www.unodc.org/documents/data-and-analysis/WDR2011/World\\_Drug\\_Report\\_2011\\_ebook.pdf](http://www.unodc.org/documents/data-and-analysis/WDR2011/World_Drug_Report_2011_ebook.pdf) [accessed 22/11/2011]. 2. Substance Abuse and Mental Health Services Administration, Office of Applied Studies. Drug Abuse Warning Network: Development of a New Design (Methodology Report) 2002. Available at: <http://www.drugabusestatistics.samhsa.gov> [accessed 22/11/2011].

### 255. Nitrous Oxide Induced Neuropathy

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**Objective:** Chronic nitrous oxide inhalant abuse can cause reversible neurologic defects including pain, paresthesias and numbness. We report three cases of nitrous oxide induced neuropathy, the clinical time course for symptom regression, and treatment considerations. **Case series:** Case 1: 29 year old male using 500 nitrous oxide canisters per day for 10–20 days, presented to the emergency department (ED) complaining of lack of sensation from mid-thigh to feet. He was ataxic, had abnormal heel to shin and difficulty raising his legs. His cranial nerve exam, lower extremity vascular status and brain MRI were normal, B12 levels were sent out and resulted normal. Two days after admission and B12 dosing, he developed bilateral upper extremity paresthesias. Over the following 3 weeks, numbness progressed to pain, prompting the patient to resume nitrous abuse. He was subsequently treated for his pain. Case 2: 43 year old female with 1.5 years of nitrous oxide use, presented with ascending numbness from her feet to her waist and recent progression to arms. MRI of her brain and spine was normal. B12 level was low (221, normal 239–931). Symptom improvement started 2 days after folate and B12 treatment. Case 3: 43 year old female using 200–300 nitrous oxide canisters per day for one year, presented confused, ataxic and desarthric without motor weakness. She also chronically used benzodiazepines and alcohol. Head CT was normal, and brain MRI showed non-specific white matter changes. Her B12 level was normal (456) and cytopenia. Vitamin B12, folic acid and multivitamins

were given, the patient was discharged on hospital day 4 without improvement of ataxia or dizziness. **Conclusion:** Chronic nitrous oxide abuse can result in reversible neuropathy, most often affecting sensory neurons of the lower extremity. There is no consensus on laboratory investigations or medical tests, but complete blood count (CBC), blood levels of B12, folate and MMA (methylmalonic acid) and homocysteine along with electromyography (EMG) and MRI brain/spine may be diagnostically helpful. Resolution can be variable, and in our experience may take weeks. Treatment should include abstaining from nitrous abuse, B12 and folate supplementation, and substance abuse counseling.

### 256. Life-Time and Recent Recreational Drug Use is Significantly Higher amongst Men Who Have Sex with Men Compared to Others Attending Genitourinary Medicine Clinics

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**Objective:** Data on the frequency of recreational drug use is collected at a population level through representative national surveys (e.g. the British Crime Survey). Anecdotally it appears that recreational drug use is more common in the men who have sex with men (MSM) community, although there is little systematic data to substantiate this. The aim of this study was to investigate the pattern of recreational drug use in patients attending a genitourinary medicine clinic and to determine whether drug use was greater amongst MSM. **Methods:** We designed a questionnaire that was given to all patients attending the genitourinary medicine clinics at two inner-city teaching hospitals over a 3 month period (July–September 2011). The questionnaire was self-completed by patients whilst waiting to see a clinician. Data was collected on age, gender, gender of sexual partner(s) and previous/current recreational drug use (type and frequency of drugs used). **Results:** 1328 questionnaires were completed; the mean  $\pm$  SD age of respondents was 30.5  $\pm$  8.5 years and 54.9% were female. 254 (19.1%) were MSM. As shown in Table 1, life-time use of all drugs except cannabis was more common in MSM and last month use of all drugs except cannabis, cocaine powder and amphetamine was more common in MSM. **Conclusion:** We have shown in this study that both life-time and last month use of most

recreational drugs are more common in MSM. There is the potential for clinical toxicologists to target this group to identify problematic use and/or to develop interventions to reduce the harm associated with recreational drug use.

### 257. Gamma-Butyrolactone, Gamma-Hydroxybutyrate Dependence

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**Objective:** Gamma-hydroxybutyrate (GHB) is an endogenous substance and an anesthetic induction agent. Since the 1970s, it has been described in cases of addiction or drug-facilitated sexual assault.<sup>1</sup> In France, GHB was scheduled as a narcotic in 1999.<sup>2</sup> Two precursors of GHB, gamma-butyrolactone (GBL) and 1,4-butanediol (BDO), are metabolized by lactonases into GHB. GBL and BDO are used as recreational drugs and are easily accessible on the industrial market and/or on the Internet. The numbers of users and cases of withdrawal have increased in many countries over the last decade.<sup>3</sup> We report three cases of GHB/GBL withdrawal and present a review of the literature. **Case series:** Three men, aged 41 to 45 years, were identified as presenting substance use disorder. Two of them attended for management of GHB/GBL dependence in a drug addiction treatment centre in Paris. Drugs were used on a daily basis for many years with increased use over the previous 6 months. Both patients described severe withdrawal symptoms in the past. The third case was a man who stopped the drug during custody and experienced a severe withdrawal reaction with anxiety, tremor, tachycardia, and sweating. Withdrawal management was based on diazepam to prevent delirium. Treatment was titrated to the severity of withdrawal symptoms. **Conclusion:** GHB/GBL use in France and European countries has increased over recent years. Both drugs seem to be attractive for drug users seeking psychoactive effects, as they are relatively inexpensive and easily accessible. Health professionals must be aware of and ensure prevention of the risks of withdrawal reaction and overdose in drug users. GBL and BDO have been banned from public sale in France since September 2011.<sup>4</sup> **References:** 1. Arrêté du 28 avril 1999 JO du 5 mai 1999. 2. Nicholson K, Balster R. GHB: a new and novel drug of abuse. *Drug Alcohol Depend* 2001; 63:1–22. 3. Galloway G, Frederick S, Staggers FE Jr, et al. Gamma-hydroxybutyrate: an emerging drug of abuse that causes physical dependence. *Addiction* 1997; 92:89–96. 4. Arrêté du 2 septembre 2011 JO du 8 septembre 2011.

### 258. Methoxetamine: A Ketamine Analogue Associated with Both Ketamine-like Dissociative Effects and Sympathomimetic Toxicity

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**Objective:** Methoxetamine is an arylcyclohexylamine analogue of ketamine that is being marketed on the Internet as a “bladder safe” derivative of ketamine, however there is currently no data to support these marketing claims. There are no reported cases of acute toxicity following analytically confirmed use of methoxetamine. **Case series:** Case One – 42 year old male was found collapsed in the street. On arrival in the emergency department (ED) he was drowsy with a Glasgow Coma Score (GCS) of 6/15, tachycardic (135 bpm), hypertensive (187/83 mmHg) and pyrexial (38.2°C). Over the next two hours, his heart rate, blood pressure and temperature returned to normal limits. He reported that prior to his collapse he had drunk three pints of beer and taken 0.75 g of “benzofury” and 0.5 g of “methoxetamine” by nasal insufflation. Case Two – 29 year old male presented having been found “catatonic” by his mother, with a tremor, visual hallucinations, confusion and dilated pupils. On arrival in the ED he was confused with a GCS of 14/15, tachycardic (121 bpm), hypertensive (201/104 mmHg). He was treated with 5 mg of oral diazepam and admitted for observation. Later he admitted that he had used 2 g of “methoxetamine” powder from an Internet research chemicals supplier. Case Three – 28 year old male brought into the ED from a local nightclub having been found collapsed; en route to hospital he developed agitation and aggression. On arrival he was drowsy with a GCS of 10/15, confused, significantly agitated, tachycardic (113 bpm), hypertensive (198/78 mmHg), with dilated pupils. His temperature was normal (36.9°C). He was treated with 5 mg of intramuscular midazolam, and his agitation, confusion and physiological features settled. Later he admitted using methoxetamine purchased from a high-street “head shop”. Toxicological screening: Serum collected at the time of presentation to the ED was analysed by gas chromatography-mass spectrometry (GC-MS). Serum concentrations of methoxetamine were 0.09–0.2 mg/L. Case 1 also had the benzofuran 6-APB/5-APB detected; no other drugs were found on an extended toxicological screen. **Conclusion:** We report here the first analytically confirmed cases of acute methoxetamine toxicity demonstrating that it is associated with both ketamine-like dissociative toxicity and also significant sympathomimetic toxicity.

### 259. Five-Year Trends in Recreational Drugs Associated with Presentation to the Emergency Department with Acute Toxicity/Harm

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**Objective:** Analysis of seized/confiscated recreational drugs in the UK has demonstrated a significant change in the availability/content of recreational drugs over the last five years. There has been a significant decrease in the availability of MDMA (‘ecstasy’), mir-

**Table 1.** Frequency of lifetime and last month use amongst the men who have sex with men (MSM) and non-MSM respondents.

	Lifetime use			Last month use		
	MSM	Non-MSM	p	MSM	Non-MSM	p
Cannabis	62.7%	58.4%	0.23	10.2%	9.2%	0.62
Cocaine (powder)	48.6%	32.8%	<0.001	4.3%	2.6%	0.14
MDMA (pill)	40.8%	30.8%	0.002	2.7%	0.9%	0.02
Mephedrone	23.9%	12.2%	<0.001	3.1%	0.1%	<0.001
Ketamine	33.7%	17.3%	<0.001	3.5%	0.5%	<0.001
Volatile nitrites	71.4%	26.9%	<0.001	18.4%	0.4%	<0.001
Sildenafil (Viagra)	43.5%	15.7%	<0.001	11.8%	0.5%	<0.001
Amphetamine	29.8%	21.2%	0.003	0.8%	0.3%	0.23
Gamma-hydroxybutyrate (GHB)	22.7%	11.1%	<0.001	2.4%	0.1%	<0.001
Gamma-butyrolactone (GBL)	16.1%	8.8%	<0.001	3.1%	0.1%	<0.001
Methamphetamine	16.9%	9.0%	<0.001	1.2%	0.2%	0.02

**Table 1.** Frequency of presentations for individual drugs per year from 2006 to 2010.

	2006	2007	2008	2009	2010
Cocaine	119	156	233	176	222
GHB/GBL	158	128	208	242	270
MDMA/Ecstasy	140	126	137	85	103
Ketamine	58	58	70	67	81
Cannabis	18	32	38	43	68
Amphetamine	14	11	24	12	22
Methamphetamine	3	3	18	22	23
Volatile nitrites	0	7	6	13	20
LSD	3	7	5	2	10
Piperazines	7	1	0	2	0
Magic mushrooms	1	3	0	1	2
Cathinones	0	0	0	18	82
Other legal highs	0	0	1	3	16

rored by an increase in availability of novel psychoactive substances ('legal highs') such as the piperazines and cathinones. There is no data as to whether similar trends are seen in the drugs associated with presentations to the Emergency Department (ED) with acute recreational drug toxicity/harm. *Methods:* Data was collated on an annual basis for all presentations to our large inner-city Emergency Department with acute toxicity relating to the self-reported use of recreational drugs between 1st January 2006 and 31st December 2010. *Results:* The frequency of drugs reported as being used by an individual presenting with acute harm is shown in Table 1. There was a significant increase in presentations associated with the use of classical drugs (cocaine, gamma-hydroxybutyrate (GHB)/gamma-butyrolactone (GBL), ketamine and cannabis) and novel psychoactive substances. Only MDMA was associated with a downward trend in presentations over the five year period. *Conclusions:* The trends seen in the ED presentation data are broadly similar to those seen in the analysis of seized/confiscated recreational drugs, particularly for MDMA and the cathinones. However, the significant increases seen in the presence of piperazines in analysis of seized/confiscated drugs were not seen in the ED presentations.

## 260. Buprenorphine/Naloxone (Suboxone) Fatality in a Child

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*Objective:* Buprenorphine/naloxone (BN; Suboxone), a combined partial mu-opioid receptor agonist and pure mu-opioid receptor antagonist, respectively, is widely used as an alternative to methadone maintenance for the treatment of opioid dependence. Since its approval by US Food and Drug Administration (FDA) in 2002, there is an increasing frequency of reports of unintentional BN exposures among children.<sup>1</sup> We report the first BN-associated death in a child. *Case report:* A previously healthy 13 month-old boy was found unresponsive and cyanotic 10–12 hours after being given a pill container of BN by one of the parents to be used as a rattle. The container was found open and several pill fragments were in his mouth. The parent removed the pill fragments and laid the child to sleep. No medical evaluation was initially sought. Approximately 10 hours later, the child was found unresponsive in his crib and emergency medical service (EMS) was notified. On arrival, EMS found the child pulseless and

apneic and performed appropriate though unsuccessful resuscitative interventions that included administration of naloxone, 4 mg. The child was declared dead upon arrival to the ED. There was no history of other ingestion and the child had no known illnesses. *Conclusion:* BN has several advantages over methadone including a theoretical ceiling effect on respiratory depression and the potential to deter IV misuse due to combined formulation with naloxone.<sup>1–3</sup> However, it is unknown if the ceiling effect also applies to children. With 1000 fold higher mu-opioid receptor affinity and 20 to 50 times greater potency compared to morphine, unintentional low dose exposure in children can result in significant adverse events including lethargy, respiratory depression and possibly death.<sup>1,2</sup> *References:* 1. Hayes BD, Klein-Schwartz W, Doyon S. Toxicity of buprenorphine overdoses in children. *Pediatrics* 2008; 121:782–6. 2. Orman JS, Keating GM. Buprenorphine/naloxone: A review of its use in the treatment of opioid dependence. *Drugs* 2009; 69:577–607. 3. Dahan A, Yassen A, Bijl H, et al. Comparison of the respiratory effects of intravenous buprenorphine and fentanyl in humans and rats. *Br J Anaesth* 2005; 94:825–34.

## 261. Aortic Dissection Due to Acute Intoxication with Mephedrone: A Case Report

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*Background:* Acute aortic dissection (AAD) is defined as a longitudinal cleavage of the aortic media by a dissecting column of blood. The incidence of AAD is estimated at 2.9 per 100,000 person-year. Mortality rate is high, and in untreated cases, reaches 1–2% per hour for the first 24–48 hours, and 90% in one year. Cocaine is a known reason for AAD, however in recent years methamphetamine and MDMA were also reported to be responsible for such cases.<sup>1,2</sup> Some authors assume that the strength of the relationship between AAD and amphetamines is stronger than for cocaine.<sup>2</sup> We describe AAD which might have been connected with chronic abuse with mephedrone. According to the best of our knowledge there are no other such cases in the medical literature. *Case report:* A 29 year old male was admitted to the hospital due to use of a higher than usual dose of mephedrone. According to the history he had been addicted to mephedrone for two years. On admission, he complained of pain in both legs and scrotum area. There were no pulses along the arteries of the lower extremities. The skin of this area was pale and cold. Blood pressure was 143/77 mmHg, heart rate 80 b/min, breath rate 20 b/min. In toxicological screening there were no other psychoactive substances like cocaine, opioids, cannabinoids and amphetamines. AngioCT showed aortic dissection and emboli in both iliac arteries. The implantation of aortic prosthesis Vaacutec 24 was performed. Because of the lack of success in embolectomy axillaro-femoral bypass was carried out. Postoperative treatment was complicated by cardiac failure, lactic acidosis, acute kidney failure and massive rhabdomyolysis which resulted in the patient's death. *Conclusion:* AAD has to be considered in patients with mephedrone abuse. Young adults with AAD should be screened not only for cocaine and amphetamine use. *References:* 1. Edwards J, Rubin RN. Aortic dissection

and cocaine abuse. *Ann Intern Med* 1987; 107:779–80. 2. Westover AN, Nakonezny PA. Aortic dissection in young adults who abuse amphetamines. *Am Heart J* 2010; 160:315–21.

## 262. Neurotoxicity Caused by Intravenous Use of Methcathinone Produced from Pseudoephedrine with the Use of Potassium Permanganate and Spirit Vinegar

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*Objective:* Illegal production and usage of methcathinone (ephedrone) from tablets containing pseudoephedrine with the use of potassium permanganate and spirit vinegar increased in Poland for the last few months.<sup>1,2</sup> *Case series:* We observed five cases of manganese induced parkinsonism (MIP) caused by intravenous use of methcathinone contaminated with manganese. All the patients presented with difficulties of speech consisting of dysarthria and stuttering. Rapidly progressing parkinsonian symptoms were observed, with pronounced stiffness, bradykinesia and loss of facial expression. Patients demonstrated also characteristic gait abnormalities with the "cock-walk" presented in two cases. Autonomic disturbances manifested as sudden pallor, excessive swallowing and orthostatic hypotonia. In two cases there were elevated levels of manganese in blood: 141 micrograms/L and 101 micrograms/L (norm: < 15 micrograms/L) despite the fact that the last injection of narcotic took place respectively four and two months previously. There was progressive worsening of symptoms in the case of a 37 year old man. In him fMRI increased signal T1 in subcortical nucleus, especially in the globus pallidus, was found. *Conclusion:* Manganese induced parkinsonism (MIP) because of its inhalation is well described, however, acute poisoning by the intravenous route is much less well known. Due to the progressive character of the neurotoxic effects of manganese poisoning the decision for detoxification with chelating agents like EDTA should be considered.<sup>1,3,4</sup> *References:* 1. Levin OS. ["Ephedron" encephalopathy]. [Article in Russian]. *Zh Nevrol Psikhiatr Im S S Korsakova* 2005; 105:12–20. 2. de Brie RMA, Gladstone RM, Strafella AP, et al. Manganese induced parkinsonism associated with methcathinone (ephedrine) abuse. *Arch Neurol* 2007; 64:886–9. 3. Huang CC, Chu NS, Lu CS, et al. Cock gait in manganese intoxication. *Mov Disord* 1997; 12:807–8. 4. Herrero Hernandez E, Discalzi G, Valentini C, et al. Follow-up of patients affected by manganese-induced Parkinsonism after treatment with CaNa2EDTA. *Neurotoxicology* 2006; 27:333–9.

## 263. Demographics, Co-Use of Illicit Drugs, and Clinical Presentation of Patients with Acute Cocaine Intoxication Presenting to a Swiss Emergency Department

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*Objective:* To describe demographics and clinical characteristics in patients presenting to an urban emer-

gency department (ED) with acute cocaine-related medical problems. *Methods:* Retrospective case-series of 166 analytically-confirmed acute cocaine intoxications admitted to the ED between January 2007 and March 2011. *Results:* Mean age  $\pm$  SD of patients was  $33 \pm 9$  years, 121 (73%) were male and 108 (65%) patients had no employment at time of presentation. Twenty-six patients (16%) abused cocaine only and 140 (84%) used at least one additional substance, most commonly opioids (45%), alcohol (41%), or cannabis (36%). The most commonly reported symptoms in the ED were chest pain in 58 patients (35%), palpitations in 33 patients (20%), anxiety in 61 patients (37%), and restlessness in 60 patients (36%). Hypertension and tachycardia were observed in 87 (52%) and 108 (65%) patients, respectively. Severe complication of cocaine abuse included 2 cases of acute myocardial infarction, one ischemic stroke, and 4 cases of generalized seizure. Most patients (124 or 75%) could be discharged home within 24 h after admission. Thirty-one patients (19%) needed emergency psychiatric evaluation. *Conclusion:* Patients presenting with acute cocaine-related medical problems to the ED were mostly young unemployed men who used cocaine together with other drugs, most often alcohol and cannabis. Co-use of other stimulants was very rarely observed. Most frequently reported signs and symptoms included hypertension, tachycardia, chest pain, palpitations, anxiety, and restlessness. Severe complications of acute cocaine use included myocardial infarction, stroke, and generalized seizure. A remarkably high number of patients needed emergency psychiatric evaluation and/or referral.

#### 264. Successful Endoscopic Removal of Cocaine Concealed in a Colostomy

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*Objective:* While concealing of containers in the rectum or vagina is common among body packers, other visceral cavities are rarely used for this purpose. *Case report:* We report on a 25-year old male patient who was admitted due to alcohol intoxication and abdominal pain during the time of Octoberfest. Physical examination of the abdomen was unremarkable with regular bowel sounds and absence of localized tenderness. Noteworthy was the existence of a colostomy on the left lower abdomen. Neurological check-up was impaired by alcohol but despite that fact unremarkable. Lab results were unremarkable except for a high blood-alcohol level (2.7 g/L) and positive screening for cocaine. The patient complained of worsening abdominal pain during the following hours. Abdomen was still soft, but the area of the colostomy exit now appeared to be swollen and painful. It was not possible to perform ultrasonic examination due to pain. The patient agreed to an x-ray of the abdomen. Abdominal film showed several foreign bodies visible near the colostomy exit. The patient confessed to being a drug courier using the colostomy as concealment for cocaine capsules ("body packing"). Due to severe abdominal pain and impaction near the colostomy exit an emergency removal was necessary. Despite several authorities recommending surgical removal, a non-surgical attempt at removal was attempted here as the capsules were seen near the colostomy exit. Finally a successful endoscopic

removal under intensive care supervision was performed. In total eight intact cocaine capsules (10 g each) were removed. Further investigation showed no remaining foreign bodies. The patient was stable during endoscopic treatment, recovered well and left the hospital the following day. *Conclusion:* Body packing is a rare cause of abdominal pain but should be considered as a differential diagnosis, especially in otherwise healthy patients. The extremely rare use of colostomy concealment for drugs and the promising non-surgical opportunities to remove these containers by experienced endoscopists should be considered in special situations. The major risk of rupture of the cocaine capsules resulting in life-threatening overdose must be considered, however.

#### 265. Gamma-Hydroxybutyrate Acute Intoxication in Italy: Recreational Drug Intoxication or Medication Overdose?

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*Objective:* Gamma-hydroxybutyrate (GHB) and analogues are known worldwide as substances of abuse and rape drugs. In Italy GHB is also a medication used in the treatment of alcohol dependence. This study evaluates a case series of GHB overdoses referred to Italian emergency departments (EDs) in order to identify the characteristics of this intoxication in our country. *Methods:* A retrospective analysis of all cases of GHB intoxication referred to the Pavia Poison Center over a four-year period (2007–2010) was performed; all cases of admission to EDs for a confirmed and voluntary GHB poisoning were evaluated, while accidental or malicious intoxications (i.e. administration by another person as rape-drug) were excluded. Characteristics of the poisoned patients and clinical features were evaluated. *Results:* 178 of the 237 cases of GHB intoxication met the inclusion criteria (M/F ratio 1.6; median age  $38.4 \pm 8.9$ ); 28% of the patients were admitted to the EDs during the weekend. Ninety-two per cent of the patients (164/178) ingested GHB in the trade pharmaceutical formulation (Alcover<sup>®</sup>). Eighty-two patients ingested only the street-GHB or the Alcover<sup>®</sup>, while other agents were co-ingested in 96 cases (53.9%), medications (78/96), substances of abuse (13/96) and ethanol (40/96) (more than two types were co-ingested in 34 cases). Severe neurological impairment (GCS < 9) was present in 56.7% of all the cases (101/178) and in 56.1% of the GHB/Alcover<sup>®</sup> pure intoxications (46/82). Agitation or seizure was present respectively in 12.4% (22/178) and in 15.8% (13/82 pure intoxications) of the cases, severe respiratory failure in 7.9% (14/178) and 6.1% (5/82). The 37.8% (62/164) of all the patients who had ingested Alcover<sup>®</sup> were in treatment with GHB for alcohol addiction. One patient died. *Conclusion:* Compared to the previously published studies on GHB intoxication, this case series shows some peculiarities such as higher average of age, high percentage of co-ingestion of medications and ethanol, lower percentage of excitatory symptoms, homogeneous distribution of the cases during the week. The use of GHB in Italy for the treatment of alcohol addiction should result in an easier availability for patients at risk of abuse and could explain the peculiarities of our case series.

#### 266. Prevalence of Intoxication by New Recreational Drugs: Preliminary Data by the Italian Network of Emergency Departments Involved in the National Early Identification System

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*Objective:* In recent years, "old drugs of abuse" have been joined by "new recreational drugs of abuse" (NeDA). The number and the severity of patients admitted to the emergency departments (EDs) for NeDA is unknown in Italy and in most cases the standard toxicological screening results are negative. The underestimation of this phenomenon could have direct implications on early diagnosis and clinical management. A study was conducted through the EDs' network referring to the Pavia Poison Centre (PPC) in order to evaluate the actual prevalence and clinical features of NeDA intoxications. *Methods:* All consecutive cases referred to the PPC (January 2010–October 2011) for suspected/confirmed substances of abuse poisoning were evaluated; cases presenting history for NeDA or atypical clinical pictures after old drugs of abuse were included. All cases were assessed for age, history, acute clinical manifestations, evolution and toxico-analytical investigations. Cocaine, opiates, cannabis, amphetamine/methamphetamine were defined as "old drugs"; all the others were considered NeDA. Ethanol intoxication and body-packers were excluded. *Results:* Among 665 cases of substances of abuse intoxication, 192/665 (29%) met the inclusion criteria. In 52/192 (27%) NeDA were declared; 7% of patients were unable to report the substances taken. The most common clinical manifestations were agitation (42%), tachycardia (37%), coma (22%), mydriasis (19%), gastrointestinal discomfort (18%) and hallucinations (14%); two fatal cases were registered. Laboratory investigations were performed in 94% of cases (181/192); 70% of biological samples/products were delivered to PPC by courier for non-urgent analysis. The NeDA identified were: MDMA (25 cases), synthetic-cannabinoids (17), ketamine (16), GHB/GBL (6), caffeine (6), atropine-scopolamine (6), butylone (2), MDPV (1), harmine/dimethyltryptamine (1), MDA (1), 4-MEC (1). *Conclusions:* The network of EDs referring to PPC and the support of the advanced toxicological analysis are useful for the identification of sentinel/atypical cases; however, this cannot quantify the phenomenon. Toxicological evaluation, the identification of lab-confirmed NeDA intoxications permits regulatory actions by the Department for Antidrug Policies (DPA) and Ministry of Health aimed at prevention and control, such as the inclusion of the NeDA in the list of controlled substances. *Acknowledgements:* Study carried out with the support of DPA – Presidency of the Council of Ministers.

### 267. Electrocardiogram Findings Suggestive of Wellens Syndrome Following Recent Cocaine Use

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**Objective:** Myocardial ischemia, secondary to coronary vasospasm, plaque rupture, or stress demand related to catecholamine release, has been reported following acute cocaine use. We describe a case of electrocardiogram findings consistent with Wellens syndrome 36 hours after reported cocaine use. **Case report:** A 22 year old man with a history of hepatitis C and polysubstance abuse presented to the Emergency Department after intravenous heroin use and naloxone administration complaining of body aches, chills, chest pain, and shortness of breath. He admitted to snorting and injecting crack cocaine 24 hours prior. He was afebrile with a blood pressure of 111/74 mm Hg, heart rate of 88 beats per minute, respiratory rate of 17 breaths per minute, and SpO<sub>2</sub> of 100% on 3 liters per minute of oxygen. Physical examination revealed pinpoint pupils, slurred speech, and track marks. His cardiopulmonary examination was normal. The electrocardiogram showed normal sinus rhythm with ST depression in leads V3, V4, and V5, and his troponin measured 0.039 ng/mL (normal: < 0.03 ng/mL). His chest x-ray was negative, and the urine drug immunoassay was positive for opiates and cocaine metabolites. He had no known family history of coronary artery disease. Within 12 hours, his symptoms resolved, troponin peaked at 0.159 ng/mL, and ECG showed biphasic T-waves in leads V2 and V3. Echocardiography revealed mild hypokinesia with an ejection fraction of 45–50% and no regional wall motion abnormalities. Cardiology did not recommend angiography due to a low suspicion for occlusive atherosclerotic disease. **Conclusion:** Wellens syndrome is characterized by biphasic or inverted T-waves in the anterior leads of the electrocardiogram and is associated with high-grade occlusion of the proximal left anterior descending coronary artery. Pseudo-Wellens, defined by classic electrocardiogram findings in the absence of occlusive disease, has been described in the setting of cocaine use and attributed to focal coronary artery vasospasm.<sup>1</sup> Healthcare providers should be cognizant of electrocardiogram findings indicative of Wellens syndrome in patients presenting with chest pain after cocaine use. **Reference:** 1. Langston W, Pollack M. Pseudo-Wellens syndrome in a cocaine abuser. *Am J Emerg Med* 2006; 24:122–3.

### 268. The Optimal Naloxone Dose in Symptomatic Children after Buprenorphine Exposure: A Case Series

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**Objective:** There are no established recommendations on the naloxone regimen to be used in children with toxic symptoms of buprenorphine exposure. In a small case series Geib et al. suggested that children with buprenorphine induced respiratory depression should receive a naloxone dose of 0.1 mg/kg IV, i.e. tenfold the dose normally required for opioid induced symptoms.<sup>1</sup> Others have reported that lower doses may be sufficient.<sup>2</sup> The Swedish Poison Centre hereby reports a case series of unintentional oral exposure of buprenorphine in small children. **Case series:** The case series consisted of eight children.

There was an equal gender distribution of the cases and ages ranged from 10 months to 6 years. According to the history, the doses ingested ranged from 2 to 32 mg, 0.2–1.78 mg/kg. All children showed symptoms within 30 to 60 minutes. The symptoms were vomiting, drowsiness or lethargy and miosis, without significant respiratory depression. The time from exposure to arrival at hospital ranged from 30 minutes to 4 hours. Naloxone was administered in all cases but the dose was known in only six of them. Three of the children received a single dose of 0.01 mg/kg IV, one received two doses (0.01 + 0.005 mg/kg) and the remaining two received continuous infusion for 12–16 hours (0.01 mg/kg/h) after an initial dose (0.01 and 0.02 mg/kg respectively). The overdose symptoms disappeared in all eight cases. **Conclusion:** Based on the present observations, titrating naloxone from an initial low dose of 0.01–0.02 mg/kg up to a full effect if needed seems to be a reasonable treatment paradigm for buprenorphine overdose in children. However, buprenorphine's high affinity to opioid receptors<sup>1,2</sup> indicates that a somewhat higher initial dose may be needed in rare cases with pronounced respiratory depression. **References:** 1. Geib AJ, Babu K, Ewald MB, et al. Adverse effects in children after unintentional buprenorphine exposure. *Pediatrics* 2006; 118:1746–51. 2. Pedapati EV, Bateman ST. Toddlers requiring intensive care unit admission following at-home exposure to buprenorphine/naloxone. *Pediatr Crit Care Med* 2011; 12:102–7.

### 269. Potentially Toxic Acetaminophen Concentration Measured After Nasal Insufflation of Percocet

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**Objective:** Abuse of prescription opioids is on the rise and a growing public health concern. Opioids may be abused via multiple routes, including nasal insufflation. Many prescription opioid products are formulated with acetaminophen raising the concern for hepatotoxicity when large doses are consumed; however, the pharmacokinetics of acetaminophen via the nasal route are poorly characterized. We report a case of a potentially toxic acetaminophen concentration after insufflation of crushed oxycodone/acetaminophen tablets. **Case report:** A 38 year-old female presented to the emergency department after two days of nasally insufflating oxycodone/acetaminophen 5/325 mg tablets. The patient reported crushing 30 tablets on the first day of use and 20 tablets on the second day of use and snorting them (total acetaminophen dose 16.25 g). She presented to the hospital on day three complaining of nausea and pharyngitis. She denied insufflating any oxycodone/acetaminophen that day and also denied oral ingestion of the drug. The patient had been admitted several times for similar presentations and endorsed chronic intranasal oxycodone/acetaminophen abuse. An initial acetaminophen concentration of 14 micrograms/mL was measured, which was potentially toxic because the patient had not insufflated any medication in almost 24 hours. Initial AST and ALT were both 8 IU/L. Due to concerns for complications secondary to chronic supratherapeutic acetaminophen exposure, the patient was admitted and a standard 21 hour course of intravenous N-acetylcysteine was administered. On hospital day two, the measured acetaminophen concentration was < 10 micrograms/mL and the patient's liver enzymes remained within normal limits. She received intravenous fluids and pain control for the marked pharyngitis and sinusitis that occurred secondary to chronic nasal insufflation of oxycodone/acetaminophen. The patient's symptoms improved after three days and she was admitted to a psychiatric facility

for drug rehabilitation. **Conclusion:** The pharmacokinetics of nasally administered acetaminophen has not been well studied, yet there is potential for significant exposure in the setting of prescription opioid abuse. Clinicians should maintain a high index of suspicion for toxicity due to adjunct medications formulated in narcotic pain preparations. **Reference:** 1. Yewell J, Haydon R, Archer S, et al. Complications of Intranasal Prescription Narcotic Abuse. *Ann Otol Rhino Laryngol* 2002; 111:174–177.

### 270. Does Cannabis Cause a Hyperemesis Syndrome?

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**Objective:** To investigate the validity of a diagnosis of the reported Cannabis Hyperemesis Syndrome. **Methods:** A clinical audit of patients referred to Western Hospital's Department of Addiction Medicine & Toxicology with a suspected diagnosis of Cannabis Hyperemesis Syndrome between July 2006 and July 2011 (five year period). Patient demographics and characteristics were obtained from a search of medical records (approved by WH Ethics) and these features then compared against the published descriptive criteria for both Cannabis Hyperemesis Syndrome and Cyclic Vomiting Syndrome. **Results:** A total of seven cases were identified; two female and five male; age range 20 – 50 years; average duration smoking cannabis of ~ 8 years. Despite increasing cannabis use (and potency available) in Australia, very few cases of suspected "Cannabis Hyperemesis" are identified in this review of a case series. None of these cases were only correlated with cannabis use; all of these cases could equally have had a diagnosis of Cyclic Vomiting Syndrome. Vomiting, GI disease, anxiety are all common in any population of substance abusers, as in this case series. Cannabis use is a high prevalence disorder which therefore may more easily be associated with many (even "rare") conditions. There appears insufficient evidence to support a diagnostic entity for "Cannabis Hyperemesis" while there is reasonable support for a "Cyclic Vomiting Syndrome" (i.e. CVS) which may provide a plausible alternative diagnosis and is supported by this case series. **Conclusion:** A diagnosis of Cannabis Hyperemesis is not supported by sufficient evidence and should be avoided; also, other diagnostic possibilities need adequate exclusion. **References:** 1. de Moore GM, Baker J, Bui T. Psychogenic vomiting complicated by marijuana abuse and spontaneous pneumomediastinum. *Aust N Z J Psychiatry* 1996; 30:290–4. 2. Allen JH, de Moore GM, Heddle R, et al. Cannabinoid hyperemesis: cyclical hyperemesis in association with chronic cannabis abuse. *Gut* 2004; 53:1566–70. 3. Fleisher DR, Gornowicz B, Adams K, et al. Cyclic Vomiting Syndrome in 41 adults: the illness, the patients and problems of management. *BMC Med* 2005; 3:20. 4. Singh E, Coyle W. Cannabinoid Hyperemesis. *Am J Gastroenterol* 2008; 103:1048–9. 5. Chang Y, Windish D. Cannabinoid Hyperemesis relieved by compulsive bathing. *Mayo Clin Proc* 2009; 84:76–8.

### 271. Agranulocytosis, Neutropenic Colitis, and Sepsis after Consumption of Levamisole Contaminated Cocaine

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**Objective:** To describe a case of agranulocytosis and neutropenic colitis after exposure to levamisole and cocaine. Levamisole is an antihelminthic agent with immunostimulating properties that was previously used as an adjuvant chemotherapeutic for colorectal cancer. **Case report:** A 49-year-old male without past medical history presented to the ED with right lower quadrant abdominal pain, nausea, anorexia, fevers, and chills. The patient appeared cachectic with a rigid abdomen and right lower quadrant tenderness. His laboratory values were remarkable for a white count of 0.9 K/cumm and an absolute neutrophil count of 0.0 K/cumm. Upon further questioning the patient admitted to snorting cocaine prior to symptom onset. Urine was obtained and was sent for detection of levamisole. This later came back positive at 1.8 micrograms/mL. A CT scan of the abdomen and pelvis was obtained showing severe thickening of the proximal ascending colon and cecum. The patient was taken to the OR where his cecum and ascending colon were noted to be ischemic and were resected. He was started on filgrastim with recovery of his cell count and was discharged after two weeks. The patient had an extensive workup during his admission and had a positive Lupus Anticoagulant, ANA, and c-ANCA and without any other source for these findings, their results were attributed to levamisole. **Conclusion:** The patient's clinical presentation appears to be linked to his use of levamisole contaminated cocaine.

#### 272. Outcomes of Suspected and Confirmed Exposures to Levamisole-Tainted Cocaine

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**Objective:** Levamisole is an antihelminthic which is used as a cocaine cutting agent. Exposure to levamisole can result in agranulocytosis. We sought to describe the initial presentation, management and outcome of patients with suspected exposure to levamisole-tainted cocaine reported to our poison centre. **Methods:** A retrospective medical record review of all cases reported to a single Canadian poison centre from April 1, 2009 to March 1, 2011 was conducted. We selected patients in whom exposure to both cocaine and levamisole were suspected based upon the history provided by the referring clinician. Data collected included the patient's initial clinical presentation, laboratory findings, treatment and outcome. **Results:** Six patients met our inclusion criteria. Four patients were positive for cocaine by urine drug screen immunoassay and two were positive for levamisole by Gas Chromatography-Mass Spectrometry. Two patients had no confirmatory testing for cocaine or levamisole but reported a history of cocaine use and were neutropenic. Five patients presented febrile (temperature > 38 degrees C) with complaints of myalgias and other nonspecific flu-like symptoms. On presentation to the Emergency Department, four patients had neutrophil counts of 0 X 10<sup>9</sup>/litre, one with 0.1 X 10<sup>9</sup>/litre and another with 0.4 X 10<sup>9</sup>/litre (normal range 2–8 X 10<sup>9</sup>/litre). Five patients received antibiotics for the following cited reasons: sepsis of unknown origin (2); myocarditis (1); wound infection (1); pharyngitis (1). Three patients received filgrastim. One patient left against medical advice on day five, two were discharged on day five and one was discharged on day ten. Two patients remained in hospital after ten days for further observation: one

for continued neutropenia and the other for cardiac monitoring. Upon discharge, five patients had normal neutrophil counts; three of these patients had received filgrastim. There were no deaths. **Conclusion:** In our study, patients with suspected or confirmed exposure to levamisole-tainted cocaine presented to hospital with features of systemic inflammatory response syndrome and neutropenia. Management included investigations for a source of sepsis, antibiotics, and filgrastim. Health care professionals should suspect levamisole toxicity in patients with a history of cocaine abuse who present with neutropenia and clinical features of sepsis.

#### 273. Oxycodone Overdose: A Case Series

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**Objective:** There are limited data on oxycodone overdose,<sup>1</sup> and it is suggested that in addition to central nervous system and respiratory depression, oxycodone may cause QT prolongation<sup>2</sup>. We investigated the clinical features, electrocardiogram (ECG) parameters and naloxone treatment of oxycodone in overdose. **Methods:** Sixty-two oxycodone overdoses were identified from admissions to a toxicology unit between February 2009 and May 2011. Demographic information, details of ingestion, ECG parameters (HR, QT, QRS), naloxone use and length of stay (LOS) were extracted from a clinical database. QT was measured manually and plotted on a QT nomogram. LOS was extracted for all overdoses over the same period. **Results:** From 62 oxycodone overdoses, 29 (47%) ingested immediate release (IR) and 33 (53%) ingested sustained release (SR) or a combination of IR/SR. Forty-nine (79%) admissions were intentional, 10 (16%) recreational and 3 (5%) non-intentional. The median age was 40 years [interquartile range (IQR): 34–50 y] and 44 were female (71%). The median dose of IR oxycodone was 80 mg (IQR: 45–110 mg; range 5–800 mg) of which one case inserted per rectum. The median dose of SR oxycodone ingested was 200 mg (IQR: 80–480 mg; range: 20–1600 mg) with two cases using it intravenously. Benzodiazepines were the most frequent co-ingested drug in 25 (40%) cases. No arrhythmias were recorded. The median QRS was 97 msec (IQR: 92–106 msec) and there were four (8%) abnormal QT-HR pairs. Naloxone boluses were required in 36 admissions (58%), and 15 (24%) required a naloxone infusion. There was higher overall naloxone use with SR (20/33 61%) compared to IR oxycodone (13/29 45%). The median length of stay was 18.3 hrs (IQR: 12.99–35.8 hrs) which was greater than the median LOS for all toxicology admissions – 15.1 h (IQR: 8.6–23.6 h) over the same period. **Conclusion:** The majority of patients were given naloxone which could account for the longer LOS in oxycodone overdoses. More in-hospital naloxone and infusions were used for the SR preparation. Oxycodone overdose was only associated with minor QT prolongation and no arrhythmias. **References:** 1. Aquina CT, Marques-Baptista A, Bridgeman P, et al. OxyContin abuse and overdose. *Postgrad Med* 2009; 121:163–7. 2. Baranchuk A, Simpson CS, Methot M, et al. Corrected QT interval prolongation after an overdose of escitalopram, morphine, oxycodone, zopiclone and benzodiazepines. *Can J Cardiol* 2008; 24:e38–40.

#### 274. Clinical Management of Illicit Drugs Body Packers: The Bergamo Poison Control Center Experience

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**Objective:** To describe initial management, complications and outcome in a series of body packer patients. **Methods:** We retrospectively reviewed the case notes, prescription charts and radiological investigations of all suspected body packers admitted to the Emergency Department (ED) of our hospital between 2009 and 2010. **Results:** We identified 53 patients (46 men, 7 women, mean age 32.3 years). The patients had all been detained at the local airport and accompanied by the customs officers; 71% were from Northern and Western Africa. The mean number of illicit drug packets was 54 (range 1–120); cocaine and hashish were the most common illegally transported substances. All patients, including a 7-week pregnant woman, underwent plain abdominal radiograph: X-ray was positive in 50 patients (94%) but in three of them it was a false positive (non-contrast CT scan excluded the presence of foreign bodies). The other 3 patients with negative X-ray underwent CT scan: 2 of them remained negative, 1 resulted positive. Conservative management (single dose activated charcoal and whole bowel irrigation) was carried out in 46 patients; only 1 patient presented vomiting because of treatment. In the other 2 patients the packets were in the rectum and there was a spontaneous emission. In selected cases, endoscopic removal of drug-filled packets was performed: 2 patients underwent gastric endoscopy and 1 rectoscopy. No patients showed clinical signs of illicit substance toxicity or bowel obstruction and no patients underwent emergency surgery. A second abdominal X-ray was performed after 3 packet-free stools were passed: discharge criteria included negative X-ray and coherence between the numbers of declared and passed packets. Three patients required abdomen and pelvis CT scans to assess the presence of the missing packets: in 2 patients history was unreliable, while in one patient CT scan resulted positive for foreign bodies. The average length of hospital stay was 28.4 hours for patients managed conservatively. **Conclusion:** Our results confirm the safety of conservative approach. The protocol used was associated with a low rate of diagnostic and therapeutic complications, and with a length of stay in hospital compatible with ED standards.

#### 275. Agitation, Hyperthermia and Multiorgan Failure after Abuse of 3,4-Methylenedioxypropylvalerone

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**Objective:** Reports of significant clinical toxicity associated with the isolated use of 3,4-methylenedioxypropylvalerone (MDPV) are lacking in the medical literature. We report a case of marked toxicity associated with “bath salt” abuse with analytical confirmation of MDPV presence and analytical exclusion of other substances of abuse. **Case report:** A 25 year-old male presented with marked agitation after injecting “bath salts” obtained via the Internet. On presentation, the patient was non-verbal with mydriasis, rightward deviation of the eyes, rubor, and combativeness. Blood pressure 148/66 mmHg, heart rate 175 beats/minute, respiratory rate 18 breaths/minute, rectal tempera-

ture 41.3° Celsius. Following intubation and mechanical ventilation, sedation was maintained with propofol. Ice packs and cooling blankets were applied. Initial significant laboratory values: white blood cell count 17,000 per mm<sup>3</sup>; potassium 5.1 mEq/L; serum bicarbonate 14 mEq/L; creatinine 2.88 mg/dL; glucose 45 mg/dL; aspartate aminotransferase 201 U/L; alanine aminotransferase 334 U/L; creatine kinase 2334 U/L; troponin 3.24 ng/mL; lactate 7 mg/dL. A head CT and cerebral spinal fluid were normal. The electrocardiogram was significant only for sinus tachycardia. Laboratory values peaked as follows: aspartate aminotransferase 16,688 U/L; alanine aminotransferase 9,085 U/L; creatine kinase 235,377 U/L; troponin 29 ng/mL. He required dialysis due to anuric renal failure. He was extubated on hospital day 9 and his mental status normalized by hospital day 13. His laboratory values all normalized with supportive care. Urine from the day of admission tested positive for MDPV at a concentration of 140 ng/mL using High Performance Liquid Chromatography/Tandem Mass Spectrometry. Blood was negative for ethanol, methanol, ethylene glycol, salicylate, and acetaminophen. Presenting urine was negative for tricyclic antidepressants, opiates, cocaine, barbiturates, marijuana, antiepileptics, 4-bromo-2,5-dimethoxyphenethylamine, 8-bromo-2,3,6,7-benzo-dihydro-difuran-ethylamine, 8-bromo-benzodifuranyl-isopropylamine, 2,5-dimethoxy-4-iodophenethylamine, 2,5-dimethoxy-4-n-propylthio-phenethylamine, 5-methoxy-N,N-diisopropyltryptamine, atropine, 1-(1,3-benzodioxol-5-yl)butan-2-amine, N-benzylpiperazine, benzylpiperazine, bufotenine, dextro/levo methorphan, ketamine, lysergic acid diethylamide, 1-(1,3-benzodioxol-5-yl)-N-methylbutan-2-amine, 4-methylmethcathinone, mescaline, methylenedioxyamphetamine, methylenedioxy-methamphetamine, methyltryptamine, dimethyltryptamine, norketamine, phenacyclidine, psilocin, salvinorin B, scopolamine, and 3-trifluoromethylphenylpiperazine. **Conclusion:** Our case is the first reported to describe clinical effects in conjunction with a positive isolated MDPV level. Our patient exhibited tachycardia, hypertension, hyperthermia, mydriasis, and severe agitation. Despite aggressive early management including intubation, sedatives, cooling measures, and dialysis, he progressed to multiorgan failure. He ultimately fully recovered.

#### 276. Market Analysis of Illicit and Emerging Drugs of Abuse in an Anonymized Internet Network

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**Objective:** The availability and supply of illicit psychoactive compounds is difficult to characterize via classical data sources. Delays in research, review, and production limit peer-reviewed material. The absence of open sources precludes conventional market research. Traditional databases assessing usage and demand often do not include emerging drugs.<sup>1,2</sup> Established government initiatives which purchase or assess illicit substances to determine supply, pricing, and purity, may not include emerging drugs.<sup>1,2</sup> **Methods:** Using the anonymous web protocol Tor, we surveyed an underground open marketplace (<http://ianxz6zefk72ulz.onion/index.php>) for illicit and novel stimulants. We recorded price, drug, amount, seller, and seller's country if declared. We then compared the price/gram to those available from previously published sources. Products with slang terms were excluded if the drug could not be verified. **Results:** The marketplace stimulant section listed twenty unique substances and nineteen unique stimulants. Fifty separate sellers were identified by handle. Declared country

of origin include the US (27%), Netherlands (19%), Canada (13%), undisclosed (13%), Germany (10%), and UK (7%). Costs/gram for following drugs (minimum, maximum, median) were: Adderal<sup>®</sup>, \$338.15, \$518.59, \$410.33; amphetamine, \$9.24, \$15.44, \$12.76; cocaine, \$73.38, \$164.34, \$97.35; synthetic cannabinoids, \$2.22, \$56.50, \$24.36; MDMA, \$28.22, \$308.18, \$56.92; methamphetamine, \$130.04, \$216.63, \$163.81; methy-lone, \$8.73, \$51.47, \$22.86; methylphenidate, \$116.00, \$425.61, \$234.06. By comparison, 2009 US prices were \$184.73 (≤ 2 grams) for cocaine and \$175.66/gram (≤ 10 grams) for methamphetamine.<sup>1</sup> Depending on country, European drug prices ranged from €10–200/gram for cocaine, €1.7–64.3/gram for synthetic amphetamines, €1–25/tablet for MDMA, and from €2.6–189/gram for methamphetamine.<sup>2</sup> **Conclusion:** Anonymous networks participate in the growing internet drug trade. Surveying underground open market websites can reveal available substances and pricing data, providing a unique opportunity to estimate market trends and scope. Clinicians and policy makers should be aware of emerging internet availability of common and novel drugs of abuse. **References:** 1. The White House. National Drug Control Strategy. Data Supplement 2011. Available at: [http://www.whitehouse.gov/sites/default/files/ondcp/policy-and-research/2011\\_data\\_supplement.pdf](http://www.whitehouse.gov/sites/default/files/ondcp/policy-and-research/2011_data_supplement.pdf) [accessed 24 Nov 2011]. 2. EMCDDA. Statistical bulletin 2011. Price and purity information (PPP). Price of cocaine products at retail level, 2009, and Price of synthetic drugs at retail level, 2009. Available at: [http://www.emcdda.europa.eu/html.cfm/index131748EN.html?type=stats&stat\\_category=w104&stat\\_type=w87&order=stat\\_reference](http://www.emcdda.europa.eu/html.cfm/index131748EN.html?type=stats&stat_category=w104&stat_type=w87&order=stat_reference) [accessed 21 Nov 2011].

#### 277. Illicit Drugs and Gamma-Hydroxybutyrate Most Common Finding in Intensive Care Unit-Treated Poisonings in Western Sweden

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**Objective:** An increasing number of poisonings with gamma-hydroxybutyrate (GHB) and other illicit drugs frequent intensive care units (ICU) in Western Sweden during recent years. The aim of this study was to study if poisoning with illicit drugs is more frequent than pharmaceuticals and to see which drugs require intensive care most frequently. **Methods:** All cases of ICU-treated poisonings during one year (2009) in the region of western Sweden were studied retrospectively via a database search. The cases were classified as intoxication with ethanol, illicit drugs, pharmaceutical drugs or other poisonings. **Results:** Two hundred and eighty three patients (171 men, 112 women) were registered with 307 visits to any of our three ICU wards during one year. Median age was 32 years with a median stay of 19 hours. Intoxication with illicit drugs was most common among men and pharmaceuticals among women. Intoxication with illicit drugs was the main diagnosis in 37 per cent of our patients, pharmaceuticals in 28 per cent, ethanol intoxication in 18 per cent, and other poisonings in 17 per cent. Illicit drugs were most common in the age group of 13–30 years as well as 31–50 years, whereas ethanol and pharmaceuticals were most common in the age group over 51. Only one death was registered (0.3%) during the initial hospital stay but within one year 12 of our patients were found to be dead (4.2%). GHB poisoning was diagnosed in 17% of all cases (n = 52). **Conclusion:** Intoxication with illicit drugs has become the most common diagnosis among poisonings in the ICU, outnumbering both alcohol intoxications and pharmaceu-

tics. Illicit drugs dominate among men and pharmaceuticals among women. The most frequent drug was GHB, which indicates a high toxicity with this drug.

#### 278. Poisonings with Narcotics and Psychoactive Drugs in Moscow. Clinical and Laboratory Parallels

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**Objective:** During the last 10 years the number of poisonings with narcotics and psychoactive drugs in Moscow has increased and according to Moscow Ambulance Station data the proportion of these rose to 20.8% of requests concerning acute poisonings. The objective is to study the structure of poisonings with narcotics and psychoactive substances used for drug intoxication in Moscow and to compare laboratory data with the clinical symptoms in order to elicit the diagnostic particulars of cases. **Methods:** Analysis of 2008–2010 annual reports of Toxicology Centers, medical history sheets and chemical and toxicological investigations performed during 2010 and six months of 2011. **Results:** During 2008–2010 2290 patients with poisoning by opiates, amphetamines, and other psychoactive drugs were hospitalized in toxicology centers in Moscow and this totalled 9.9% of all poisoned patients admitted to the mentioned centers. Biomedica of 236 patients with a medical history of use of opiates (128 patients), cannabinoids (27), amphetamines (20), phenobarbital (20) and other psychoactive drugs were examined by gas chromatography-mass spectrometry. There were 60 cases (25.4%) in which only one substance of abuse was determined, the other 169 showed several combinations including from 2 to 6 substances in each sample e.g. 6-monoacetylmorphine, morphine, codeine, methadone, tramadol, amphetamine, cannabinoids, barbiturates, benzodiazepines, tropicamide, Phenibut (aminophenylbutyric acid) etc. The combination of 6-monoacetylmorphine, morphine and codeine was considered to be as a result of use of heroin. Codeine or morphine in combination with ibuprofen or sodium methamizol was determined in 14 cases and afforded grounds to consider that those were cases of the home prepared substance “dezomorphine”. Complete clinical and laboratory results were in agreement in only 60 (25.4%) cases. **Results:** Opiates and cannabinoids prevail in the group of patients admitted to the toxicology centers for poisoning with narcotics and psychoactive drugs. Clinical symptoms of poisoning corresponded to laboratory examination data only in 25.4% of cases. Chemical and toxicological laboratory analysis confirmed in 74.6% of cases the combination of from 2 to 6 substances of abuse that had an effect on clinical symptoms. In our opinion laboratory examination is obligatory for all cases of such poisoning as it helps to achieve a precise diagnosis and to get actual information of the abused substances.

#### 279. Hawaiian Baby Wood Rose Seeds: A Case Series

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**Objective:** *Argyrea nervosa* (Hawaiian baby woodrose, HBW) seeds are easily available over the Internet or

can be purchased from 'Head Shops'. These seeds are used for their psychoactive effects and have become more popular in recent years, however, only a few case reports have been published. Therefore we retrospectively studied all cases received at the Swedish Poisons Information Centre (Swedish PC) from January 2000 until December 2010, a ten year time period. *Case series:* The Swedish PC has been consulted in 65 cases relating to abuse of HBW seeds or seeds suspected to be HBW. The dose was known in 43 cases and varied between 4–30 seeds. Hospitals consulted the poisons centre in 34 cases. The most common symptoms were nausea/vomiting (29/65 cases), hallucinations (14/65 cases), mydriasis (14/65 cases), tachycardia (12/65 cases), and agitation (10/65 cases). A number of other less common symptoms e.g. diarrhoea, headache, CNS-depression and tremor were noted. Some discrepancies e.g. seizures, leucocytosis and elevated transaminases were also found. Specific anticholinergic symptoms were only found in one case (dry mouth). Most of the intoxications were mild or moderate and no severe cases occurred. When treatment was needed, sedation with benzodiazepines was normally sufficient; however, in a few cases propofol was added. Effects noted in our study are supported by the literature,<sup>1,2</sup> but can be variable most likely due to large differences in alkaloid content (mainly lysergic acid amide (LSA))<sup>3</sup>. *Conclusion:* Our study shows that ingestion of Hawaiian Baby Woodrose seeds mainly causes mild or moderate symptoms, very similar to other hallucinogens, e.g. LSD, and hallucinogenic tryptamines. Supportive treatment and benzodiazepines are normally sufficient. *References:* 1. Furbee RB, Curry SC, Kunkle DB. Ingestion of *Argyrea nervosa* seeds. *Vet Hum Toxicol* 1991; 33:370 [abstract]. 2. Göpel C, Maras A, Schmidt MH. Hawaiian baby rose wood: case report of an argyrea nervosa induced psychosis [Article in German]. *Psychiatr Prax* 2003; 30:223–4. 3. Kremer C, Paulke A, Wunder C, et al. Variable adverse effects in subjects after ingestion of equal doses of *Argyrea nervosa* seeds. *Forensic Sci Int* 2012; 214:e6–8.

#### 280. 4-Hydroxy-Methylethyltryptamine: A Case Series and Some Analytically Confirmed Cases

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*Objective:* The hallucinogenic tryptamine, 4-hydroxy-methylethyltryptamine (4-HO-MET) is a novel recreational drug. In Sweden, 4-HO-MET is not yet legally controlled, therefore it can easily be purchased on the Internet. There are no published reports regarding poisonings after recreational abuse of 4-HO-MET. We performed a retrospective study analyzing all cases reported to the Swedish Poisons Information Centre (PC) from January 1, 2008 until November 14, 2011. If urine samples were collected from a patient with a history of 4-HO-MET use, they were analysed by GC-MS. *Case series:* 60 cases were reported to the Swedish PC. Adolescents and young adults (< 30) were involved in at least 45 of these cases. Eleven cases had both a history of 4-HO-MET use and a urine sample was available. Eight of these were positive for 4-HO-MET. Another four positive urine samples came from cases where 4-HO-MET intake was not suspected. In total 12 cases were analytically confirmed and seven of these were positive for 4-HO-MET alone. The other five were mixed poisonings with one or several additional substances (benzodiazepines, cannabis, ethanol, flephedrone, 3-fluoromethylcathinone, JWH-015, JWH-210 and tramadol). In three cases 4-HO-MET

was also confirmed in confiscated powder material. A few cases were positive for amphetamine and cocaine on urine dip-sticks without these being confirmed by GC-MS analysis. In all 60 cases the most commonly observed symptoms were mydriasis (32/60, 53%), agitation (25/60, 42%), tachycardia (26/60, 43%), hallucinations (21/60, 35%) and confusion (18/60, 30%). In the 4-HO-MET alone positive group, these symptoms were even more frequent: mydriasis (100%), agitation (83%) tachycardia (67%) and hallucinations (33%). In five of the analytically confirmed 4-HO-MET cases the poisoning severity score was graded as moderate (PSS 2), seven were graded as mild (PSS 1), but no severe or lethal cases were found. Supportive treatment was sufficient in most cases, but some cases needed sedation with diazepam and sometimes even addition of propofol. *Conclusion:* These are the first cases presented regarding the novel recreational substance 4-HO-MET. In our retrospective study mild or moderate hallucinogenic effects and sympathomimetic symptoms were noted. Symptomatic treatment with the addition of benzodiazepines was normally adequate but in a few cases propofol was needed.

#### 281. Comparison of Toxicity from Exposures to Buprenorphine or Methadone with and without Benzodiazepines

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*Objective:* Polysubstance use is prevalent in individuals using buprenorphine or methadone, with benzodiazepines being a common co-ingestant. The objective of this study is to compare the severity of buprenorphine and methadone toxicity with and without co-ingestion of benzodiazepines. *Methods:* A retrospective analysis of buprenorphine and methadone cases from 11–1–02 to 12–31–10 reported to the Maryland Poison Center was conducted. Inclusion criteria: age 18 years and older, exposure to buprenorphine or methadone with or without benzodiazepines. Cases with other co-ingestants were excluded. Outcome measures were clinical effects, treatments, disposition and coded medical outcomes. *Results:* Of 590 cases meeting inclusion criteria, 56% were male. The proportion of cases involving co-ingestion of benzodiazepines was significantly higher for methadone than buprenorphine ( $p = 0.004$ ). In 45% of cases the exposure resulted from non-medical use (intentional misuse or abuse). Table 1 compares frequency of specific clinical effects. Naloxone was used in < 5% of buprenorphine-related cases but was administered to 170 (53.3%) methadone-only and 79 (68.7%) methadone-benzodiazepine cases.

**Table 1.** Frequency of specific clinical effects for exposures to buprenorphine and methadone with and without benzodiazepines.

Clinical Effects	Buprenorphine Groups		Methadone Groups	
	Buprenorphine-only N = 133 (%)	Buprenorphine-Benzodiazepine N = 23 (%)	Methadone-only N = 319 (%)	Methadone-Benzodiazepine N = 115 (%)
Drowsy/lethargy	23 (17.3)*†	13 (56.5)*	158 (49.5)*†	78 (67.8)*
Coma	3 (2.3)†	3 (13.0)	78 (24)*†	40 (35)*
Respiratory depression	4 (3.0)	4 (17.4)	78 (24.5)	30 (26.1)
Abdominal pain	11 (8.3)	0	1 (0.3)	0
Vomiting	16 (12.0)	0	24 (7.5)	9 (7.8)
Diaphoresis	8 (6.0)	0	6 (1.9)	0

\*significantly different within groups; †significantly different between groups.

Admission to critical care was required for none of the buprenorphine-only, 4 (17.4%) buprenorphine-benzodiazepine, 94 (29.5%) methadone-only and 40 (34.8%) methadone-benzodiazepine cases. There was no difference in distribution of coded medical outcomes for buprenorphine-only vs buprenorphine-benzodiazepine and for methadone-only vs methadone-benzodiazepine. However, outcomes were more serious for methadone groups compared to buprenorphine groups. There were 7 methadone-related deaths (5 methadone-only) and no buprenorphine deaths. *Conclusion:* Buprenorphine is safer than methadone whether these drugs are taken alone or in combination with benzodiazepines.

#### 282. Role of P-Glycoprotein in the Acquisition of a Tolerance to the Respiratory and Analgesic Effects of Buprenorphine in Mice

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*Objective:* Buprenorphine (BUP) and morphine are two potent opioids largely prescribed as analgesics. Both are responsible for acute overdoses with respiratory depression in chronically treated patients, possibly attributed to the development of a tolerance to their analgesic effects requiring the administration of increased doses. Our objective was to evaluate the development of a tolerance to BUP analgesic and respiratory effects, following repeated treatment with BUP (direct tolerance) or morphine (cross-tolerance). We studied the role of P-glycoprotein (P-gp), a transporter at the blood-brain barrier, in the development of this tolerance. *Methods:* Wild and P-gp knock-out (KO) FVB mice were subcutaneously treated during 10 days with BUP (1.2 mg/kg), morphine (2.5 mg/kg) or NaCl 0.9% (control group) till the day before the test. The effects of increasing BUP doses administered intraperitoneally (IP) to the animals were studied at 30 min post-injection using the hotplate test (analgesia) and plethysmography (respiratory effects). *Results:* We assessed the ceiling effects of BUP at elevated doses with inversed U-form dose/effect relationships. Repeated BUP treatment induced a tolerance to BUP-related analgesia (significant delay to licking) as well as respiratory effects (significant reduction in the increase of the inspiratory time). There was no cross-tolerance with morphine. The effects were significantly more reduced in KO in comparison to wild-type mice ( $p < 0.05$  for 2 mg/kg BUP dose). Moreover, no tolerance was observed following the repeated administration of BUP in KO mice. *Conclusion:* Tolerance to BUP-

related analgesic and respiratory effects is observed after repeated BUP administration without any cross-tolerance with morphine. P-gp suppression is able to reduce these effects, resulting in a more limited tolerance. Our results suggest that P-gp may play a key-role in BUP activity and in the development of a tolerance for its analgesic and respiratory effects. However, the exact molecular mechanism of P-gp involvement remains to be assessed.

### 283. Which Advantages Does a Buprenorphine/Naloxone Combination Have in Comparison to Buprenorphine Alone Regarding Respiratory Effects?

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**Objective:** In drug addicts, fatal overdoses have been attributed to buprenorphine (BUP) intravenous (IV) misuse and association with benzodiazepines (BZD). Thus, a combination of BUP and naloxone (NLX) has been marketed as maintenance treatment to replace BUP alone, aiming to dissuade drug addicts from injecting crushed pills resulting in acute withdrawal syndrome. To date, the definitive benefit of this association is unclear. Our objectives were to study the respiratory effects of BUP/NLX combination in comparison to BUP. **Methods:** Using plethysmography, we studied the respiratory effects of BUP/NLX in different conditions of administration in Sprague-Dawley rats: alone, in association with diazepam (DZP), and in BUP-dependent rats (obtained by repeated SC pretreatment with 1 mg/kg BUP during 14 days). We have chosen elevated doses of BUP (30 mg/kg) and DZP (20 mg/kg) and BUP/NLX ratio of 1:4 to be equivalent to the marketed product. Reversion of DZP effects was tested using IV 10 mg/kg flumazenil. **Results:** BUP/NLX as well as BUP alone did not result in any significant respiratory depression, while their association with DZP was responsible for a significant decrease in the minute ventilation in comparison to controls. NLX prevented BUP-related increase of inspiratory time in naive rats but did not avoid BUP + DZP-related respiratory depression. These deleterious effects were reversed by flumazenil, as expected by its pharmacodynamic nature and GABA-A receptor involvement. Repeated BUP injections resulted in the development of tolerance to its respiratory effects, evidenced by the disappearance of the significant increase in inspiratory time. In tolerant rats, BUP/NLX combination induced a significant withdrawal syndrome but protected the animal against the acute toxicity that resulted in the death of all animals receiving BUP alone. Interestingly, BUP/NLX + DZP combination was not responsible for any respiratory depression. **Conclusion:** In rats, the BUP/NLX combination exhibits some advantages in comparison to BUP: protection against the risk of toxicity in relation to BUP injection and attenuation of BUP/BZD-related deleterious effects in tolerant rats. However, these benefits have yet to be assessed in humans.

### 284. The Evaluation of Insulin Sensitivity Disturbances in Ethanol Dependence and Withdrawal

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**Objective:** The aim of this study was to assess insulin resistance in ethanol dependent patients and to examine the risk of development of insulin resistance in relation to the intensity of the alcohol withdrawal syndrome. **Methods:** The study group comprised of 88 males, aged from 21 to 50 years (39.2 ± 7.8) treated for ethanol withdrawal syndrome. Diabetes, liver, kidney and pancreatic diseases were excluded by biochemical tests and ultrasonography. Body mass index (BMI) was calculated. The intensity of the withdrawal symptoms was evaluated according to the CIWA-Ar scale. Blood glucose and insulin levels were determined after fasting and at the 0, 60th and 120th minute of an oral glucose tolerance test (OGTT). Insulin resistance was defined using the insulin resistance indices, in which fasting insulin level and insulin level at the 120th minute of OGTT and Homeostasis Model of Assessment – Insulin Resistance (HOMA-IR) were analysed. **Results:** Normal BMI was calculated in 63.6% of patients, whereas obesity was detected only in 7.95%. Ethanol withdrawal syndrome was diagnosed as severe in 42% of examined patients and as moderate in 58%. Insulin resistance was detected in 17.44% of patients as assessed by their fasting glucose level (0 min) in OGTT and in 20.23% of patients when their glucose level at the 120th min of OGTT was analysed. Based on the HOMA-IR index, insulin resistance was diagnosed in 18.82% of patients. The monomial regression of log-transformed data revealed that BMI was the risk factor for fasting insulin resistance (OR = 1.17, p = 0.02) and HOMA-IR-based insulin resistance (OR = 1.24, p = 0.005), especially in the obese subgroup (fasting: OR = 8, p = 0.01; HOMA-IR: OR = 13.33, p = 0.004). Impaired glucose tolerance (OR = 4.5, p = 0.03) and diabetes (OR = 6.3, p = 0.04) in OGTT were additional risk factors. The duration of ethanol addiction (OR = 1.02, p = NS) and intensity of withdrawal syndrome (OR = 1.27, p = NS) were not risk factors for insulin resistance. **Conclusions:** BMI was the risk factor of fasting insulin resistance and HOMA-IR-based insulin resistance. Insulin resistance diagnosed on the basis of the HOMA-IR index was statistically significantly more frequent in obese patients.

### 285. Carbohydrate Metabolism Disturbances in Ethanol Dependence and Withdrawal

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**Objective:** The aim of the study was to assess the risk factors of type 2 diabetes in ethanol dependent patients and to evaluate the disturbances of carbohydrate metabolism in ethanol withdrawal syndrome. **Methods:** The study group comprised of 88 males, aged from 21 to 50 years (39.2 ± 7.8) treated for ethanol withdrawal syndrome. Diabetes, liver, kidney and pancreatic diseases were excluded by biochemical tests and ultrasonography. Body mass index (BMI) was calculated. The intensity of the withdrawal symptoms was evaluated according to the CIWA-Ar scale. Blood glucose was determined after fasting and at the 0, 60th and 120th minute of an oral glucose tolerance test (OGTT). The patients were classified according to OGTT **Results:** diabetes, impaired glucose tolerance (IGT), impaired fasting glycaemia (IFG) and normal glucose tolerance. **Results:** The mean duration of ethanol addiction was

10.6 ± 7.2 years. Ethanol withdrawal syndrome was diagnosed as severe in 42% of examined patients and as moderate in 58%. Normal BMI was calculated in 63.6% of patients, whereas obesity was detected only in 7.95%. At the 120th min of OGTT diabetes was found in 10.23% and hypoglycaemia in 11.36% of the study group. IFG and/or IGT were noted in 23.86% of the patients. There was a statistically significant relationship between BMI and diabetes (p = 0.05). A greater frequency of diabetes correlated with a lower BMI. A higher frequency of hypoglycaemia was confirmed in patients preferring to drink strong alcohol e.g. vodka (p = 0.04). Polynomial regression of log-transformed data for the risk of type 2 diabetes demonstrated that the intensity of withdrawal symptoms according to the CIWA-Ar scale (OR = 1.59, p = 0.05) and the duration of alcohol consumption (OR = 1.01, p = 0.03) were risk factors for the development of type 2 diabetes. Greater BMI was a protective factor against diabetes in the study group (OR = 0.49, p = 0.02). **Conclusions:** Incidences of diabetes and hypoglycaemia at the 120th min of OGTT were similar. The risk of diabetes was inversely proportional to BMI value. Risk factors of type 2 diabetes included the duration of alcohol consumption prior to admission and the intensity of withdrawal symptoms according to the CIWA-Ar scale.

### 286. Racial and Gender Differences in Alcohol-Related Seizures

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**Objective:** Alcohol is the most commonly abused drug in the US. Although alcoholism affects men and women of all races and ages, we hypothesized that alcohol-related seizures are heterogeneously distributed. **Methods:** A one-year retrospective review of adults admitted to one large urban hospital was conducted. Patients were eligible if they had simultaneous ICD-9 codes for both alcohol and seizure related diagnoses. Subjects were compared to two historical controls: 1) All adult Emergency Department (ED) patients over a 6-month period; 2) 577 ED alcoholics defined by their responses to the CAGE questionnaire. Patients were excluded for erroneous coding, not having the seizure admission concurrent with the alcohol-related diagnosis and incomplete charting. Bivariate correlations, paired T tests and Z scores were used to evaluate the data. **Results:** Of 3608 admissions with ICD-9 codes for alcohol or seizure diagnoses 85 met final inclusion criteria. Subjects were predominately male (92%), 72% were 41–60 years old. Racial breakdown was: White 38%; Black 23%; Hispanic 30%; and Other 7%. Compared to historical controls of general ED patients, alcoholic patients were more often Black (46% vs 25%) or White (28% vs 19%), and less often Hispanic (24% vs 36%) or other races (2.6% vs 20%). In contrast, when patients with alcohol-related seizures were compared to the ED alcoholics (CAGE +) without seizures they were more often White (39% vs 28%) and less often Black (24% vs 46%). Women were disproportionately under-represented in all alcohol groups compared to the control group of general ED patients. Z scores indicate that Whites were more likely to suffer alcohol related seizure (1.02) along with Other races (1.33) when compared with the 2 control groups (0.4 ED and 0.05 CAGE

for Whites, 1.06 ED and 1.06 CAGE for Other). Hispanics (0.41) and Blacks (0.11) were less likely to have seizures when compared with controls (1.29 ED and 0.22 CAGE for Hispanics; 0.17 ED and 1.3 CAGE for Blacks). **Conclusion:** In this study population, alcohol-related seizures occurred more frequently in older white males, despite this group not being the prominent subset of alcoholics. These differences may be pharmacogenetic in origin and warrant further investigation.

### 287. High Dose of Hydroxocobalamin Reverses Tobacco-Alcohol-Amblyopia within One Day

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**Objective:** In the late 16th century tobacco smoking was brought to Europe by English buccaniers. Already in 1604 King James I described the first problems with vision in a treatise: "A Counterblaste to tobacco". A suspicion arose that abuse of alcohol, heavy smoking and malnutrition were responsible for blindness which was called tobacco-alcohol-amblyopia. The disease was common in the 19th and at the beginning of the 20th century and has become very rare nowadays. This may point to the importance of malnutrition in causation of this disease which can rarely be seen in Europe today. The idea was that a lack of Vitamin B12 leads to an impaired detoxification of cyanide generated by smoking. Slow improvement was seen after cessation of smoking plus low dose supplementation of Vitamin B12. **Case report:** A 43 old male with a body mass index (BMI) of 16, drinking 2 liters of cheap red wine and smoking 30 cigarettes a day for most of his life went almost blind over 2 days starting with colour blindness. He went to the ophthalmologist as he could only see contours. On examination his visual faculty was down to 3% (1/30). An absolute central scotoma was found. The fundus was normal. The visual evoked potentials (VEP) were delayed. He was transferred to our department. The laboratory findings pointed to severe alcoholism: Gamma-GT 1 450 U/L, MCV 103 fl, GPT 232 U/L. He had stopped smoking and drinking for 2 days. Ethanol in blood was zero, HCN 0.11 mg/L, vitamin B12 was in the normal range. He was treated with 2.5 g hydroxocobalamin IV. The next day he claimed to see as well as before and was able to read the newspaper. The visual acuity had improved to 30% on the right eye and to 50% on the left eye and has not improved further since. **Conclusion:** Tobacco-alcohol-amblyopia is a disease of which the pathogenesis is not well understood. It is a toxic optic neuropathy most likely due to chronic cyanide poisoning of the N. Opticus. Usually improvement is slow under low dose Vitamin B 12 supplementation. High dose hydroxocobalamin – which to our knowledge was not used so far – seems to improve this disorder rapidly.

### 288. A Randomized Controlled Trial of a Community Based Alcohol Education Program in Changing the Drinking Pattern in Rural Sri Lanka

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**Objective:** To assess the effectiveness and acceptability of a brief community based educational program

on changing the drinking pattern of alcohol in a rural community. **Methods:** A randomized controlled trial in two rural villages in Sri Lanka. The intervention village received a community education program that utilised street drama, poster campaigns, leaflets, and individual and group discussions. The control village had no intervention during this period. The Alcohol Use Disorder Identification Test (AUDIT) was administered by trained interviewers to measure drinking pattern before and at 6 and 24 months after the intervention in males over 18 years of age in both villages. The recall and impact of various components of the intervention was assessed at 24 months post intervention. The primary analysis was of the study populations AUDIT score at baseline and then the differences in scores compared to the individual's baseline at 6 months and at 24 months with Mann-Whitney test and linear regression of change in scores compared with baseline scores. **Results:** Baseline drinking patterns and AUDIT scores were recorded from 246 males but were not significantly different between villages. There was a significant reduction in the AUDIT scores in the intervention village compared with the control at 6 and 24 months ( $p < 0.0001$ ). In the intervention village this was associated with the sustained development of a community action group and a significant reduction in illicit alcohol outlets. The recall of the intervention was very high for the baseline medical clinic (93%), street drama (85%) and poster (75%) whereas the leaflets (43%) and brief intervention (52%) were less well recalled. The preferred intervention by the community was the street drama with 75% approval with the other interventions being less than 15%. **Conclusion:** A community based education program had high acceptance and produced a significant reduction in alcohol use that was sustained for two years.

### 289. Baclofen and Alcohol Dependence: A Treatment at Risk?

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**Objective:** Baclofen is a centrally acting muscle relaxant with GABA-B agonist and possibly, dopamine antagonist activities. When orally administered, it should be used in incremental doses to avoid side effects. Since the 2000s, studies have attempted to show its efficacy for alcohol dependence treatment. In October 2008 a French physician published "The last glass": a book relating a successful self-experiment of baclofen in high doses (up to 270 mg/day, orally) for alcohol withdrawal. In these contexts of wide media coverage, significant risk of side effects and increasing off-label use, the French Health Products Safety Agency requested the National Coordination Committee for Toxicovigilance to assess the possible impact on case notification to the French Poison and Toxicovigilance Centres (FPTCs). **Methods:** A retrospective study analyzed all cases of exposure to baclofen collected over the period 2000–2010 by the FPTCs; their circumstances and severity (defined by the presence of convulsions, coma, collapse, arrhythmias, cardiac arrest, acute pulmonary edema, bradypnea/apnea, respiratory distress or death) were analyzed. Adjustments were made, taking into account the activity of FPTCs and sale data. **Results:**

Baclofen sales increased (+ 108% from 2000 to 2010), indicating an increased number of patients treated, particularly between 2007 and 2010. In FPTCs, 735 cases of exposure associated with baclofen were collected (45% symptomatic, 16% severe, 0.4% fatal cases), 32.7% resulted from a suicide attempt (86.7%, 44.6% and 1.3% respectively) and 44.9% from therapeutic use (21.2%, 1.2% and 0% respectively). The time course of annually reported cases showed an increase in both circumstances, mainly from 2008, which persisted after adjusting for FPTCs activity and/or baclofen sales. For severe cases, an increase was also observed, but for suicide attempts only. **Conclusion:** A sales increase following the book publication is consistent with the hypothesis of an increase in baclofen prescriptions outside the intended indications. It can explain the associated increase in cases reported to the FPTCs. The concomitant increase in severe cases after suicide attempts could result from a greater availability of baclofen to a population of patients with alcohol dependence, more likely to be at risk of depression or suicide attempt.

### 290. Fatalities Due to Acute Methanol Intoxication: A Ten Year Study

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**Objective:** To examine methanol poisoning cases and to define the demographic features and determine the mortality rates of patients. **Methods:** The records of the Toxicology Clinic, Emergency Hospital "N.I.Pirogov" were reviewed retrospectively for all methanol poisonings during a 10 year period – from January 1, 2001 to December 31, 2010. The patient's age, gender, blood methanol level and the outcome of intoxication were recorded. **Results:** There were 44 patients, hospitalized in the Clinic, due to methanol poisoning during that period of time. There were 32 men (73%) and 12 women (27%); median age 52 (range 28–76) years. The largest age group was 41 – 50 year olds (36.36%). The reason for ingestion was accidental in 35 cases – 80%, (27 men and 8 women), suicide attempt in 9 cases – 20%, (5 men and 4 women). The blood methanol concentrations ranged widely from 0.1 to 5.1 g/L. The number of deaths due to methanol poisoning was 33 (75%) and survivors – 11 (25%) during that period of time. Average concentration of methanol for patients with fatal outcomes was  $1.43 \pm 1.28$  g/L and for survivors  $0.73 \pm 0.6$  g/L. Conventional treatment of methanol intoxication was used: dialysis, parenteral infusions of bicarbonate and 95° ethanol containing solution as antidote. **Conclusion:** Methanol poisoning is an extremely hazardous form of intoxication, but survival with high blood methanol concentration is possible. Rapid analysis, early adequate treatment and receiving ethanol as an antidote were important for a favorable outcome. This compound is readily dialyzable and an antidote exists to prevent metabolism to more toxic compounds.

### 291. Risk Assessment Score for Methanol Poisoning

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**Objective:** There are outbreaks and clusters of methanol poisoning where both epidemiological and clinical parameters are reported, but most reports are either smaller case series, or they are lacking in detailed parameters such as serum methanol analysis and even arterial blood gases. Based on a large amount of information on methanol patients from six different outbreaks/centres in five different countries, we made a simple risk assessment score based on clinical parameters and arterial blood gas on admission only. **Methods:** The material was collected from two different outbreaks in Norway (1979 and 2002–2004), one outbreak in Estonia (2001), one in Tunisia (2003/2004), as well as material from two centers in Iran (Logham-Hakim Hospital in 2004–2008 and Mashhad University Hospital in 2009–2010). The inclusion criterion was: patients admitted to hospital alive with a suspected diagnosis of methanol poisoning, where a blood gas analysis was drawn on admission. The definite diagnosis should be obtained on admission, or later, by a positive S-methanol. **Results:** pH was found to be the most important prognostic marker, followed by coma and finally the ability to lower the pCO<sub>2</sub> values, most probably due to hyperventilation. HCO<sub>3</sub><sup>-</sup> and base deficit also had a prognostic value, but they were both dependent on pH. Based on the large number of patients and on those three most important parameters we made a risk-assessment scheme and a corresponding score to create a simple tool for evaluating the outcome of the patients from admission data only. **Conclusion:** The risk assessment scheme could be useful in triaging patients in larger outbreaks with a lot of victims in a short time span, as well as giving a prognostic clue for methanol poisonings in general.

### 292. Assessment of Severity and Prognosis of Methanol Poisonings

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**Objective:** Methanol poisonings in Bulgaria are usually severe and with extremely high lethality. The reason is the late start of medical treatment when extreme metabolic acidosis has already caused fatal damage. Cases with an early start to treatment post methanol ingestion are rare. **Case series:** We present two cases of acute methanol poisoning with high levels of methanol on admission, who survived intoxication. Case I – 53 year old male, who attempted suicide with methanol and clonazepam, was found unconscious two hours post ingestion and was hospitalized one hour later. Case II – 52 year old male with chronic alcohol consumption ingested wood spirits and about 12 hours later complained of headache, blurred vision and unsteady gait. He was hospitalized 16 hours later. Basic laboratory results (blood methanol and ethanol levels, blood gases, etc) are presented in Table 1. Treatment included hemodialysis, antidote – ethanol 1 mL/kg loading dose, followed by a dose of 1 mL/kg/hour, alkalization as per accepted standards (for case II). Both patients were discharged healthy on day 21 and 4 post hospitalization, respectively. **Conclusion:** Case I developed only cerebrototoxic effects of methanol (in combination with clonazepam effects) without significant acidosis due to insufficient time for its conver-

**Table 1.** Laboratory results for methanol poisonings.

Case	I					II			
	3h	21h	43h	69h	93h	16h	32h	38h	62h
Time post-ingestion (in hours)									
Blood pH	7.27	7.31	7.35	7.37	7.43	7.10	7.31	7.36	7.38
Base excess (mmol/L)	-14.0	-5.9	-6.0	-7.0	-1.1	-22	-13	-7	-2
Blood methanol (mg/mL)	5.06	2.57	1.23	0.44	0.00	1.99	0.88	0.34	0.00
Blood ethanol (mg/mL)	0.53	0.05	0.07	0.10	0.01	0.00	0.94	0.11	0.00
Hemodialysis	Yes	Yes	Yes	No	No	Yes	Yes	No	No

sion to formic acid. Case II was admitted with signs of poisoning with moderate metabolic acidosis. Early start of detox-depurative and antidote treatment prevented further development of signs and symptoms of methanol intoxication. Severity and outcome of methanol poisoning should be assessed based on severity of metabolic acidosis and not on blood methanol level.

### 293. Detectable Serum Ethylene Glycol Levels after Subcutaneous Injection of Antifreeze

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**Objective:** Poisoning from ethylene glycol (EG) ingestion and data supporting the improbability of toxicity from inhalational or dermal exposure to EG are well described. However, there is a paucity of data regarding systemic absorption or development of toxicity in humans after subcutaneous injection of EG. We present two cases of subcutaneously injected EG-containing antifreeze resulting in elevated serum EG levels. **Case series:** Two women presented to a hospital after injecting EG into their abdomens in divided doses in a suicide attempt. They believed that EG injected directly into fat would expedite death. Patient A, a 24 y/o with a history of anxiety, depression and previous suicide attempts, injected 40 mL of EG-containing antifreeze subcutaneously using four syringes. Serum EG levels were measured on arrival (51 mg/dL), morning of hospital day (HD) 2 (53 mg/dL), evening of HD 2 (37 mg/dL), HD 3 (21 mg/dL), and HD 4 (13 mg/dL). Her lowest serum bicarbonate was on arrival (17 mEq/L) and highest creatinine was 0.8 mg/dL. Patient B, 35 y/o, also attempted suicide with Patient A by injecting 60 mL of EG-containing antifreeze subcutaneously with six different syringes, as well as, ingesting an unknown amount of clonazepam and eszopiclone. She had multiple medical problems including bipolar disorder and previous overdose. Serum EG levels were measured on arrival (55 mg/dL), HD 2 (34 mg/dL), and HD 3 (17 mg/dL). Her lowest serum bicarbonate was on HD 2 (14 mEq/L) and highest creatinine was 0.9 mg/dL. Both patients were initially altered, confused, and combative. They received fomepizole, thiamine, and were intubated for less than 48 hours after developing sedation shortly after presentation. Toxicology screens at time of arrival were negative for ethanol, salicylate, and acetaminophen in both patients. A urine drug screen was positive for benzodiazepines in Patient B but completely negative in Patient A. Ultimately, both recovered fully without any lasting end organ effects and adamantly denied ingesting EG orally. **Conclusion:** While research is needed to better establish the pharmacokinetics of subcutaneous EG toxicity, these cases demonstrate previously unreported subcutaneous injection of EG resulting in systemic absorption.

### 294. Boys Will be Boys: Seizures and Shoulder Dislocations after C4 (Cyclonite) Ingestion

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**Objective:** C4 contains 91% cyclonite, which has been implicated in a multitude of clinical effects such as seizures, intoxication, vomiting, syncope, dizziness, leukocytosis, renal failure, hypotension and bradycardia<sup>1</sup>. No deaths have been reported to date and clinical effects typically resolve within a few days. Despite known side effects, military personnel continue to ingest small pieces of this material to experience reported euphoric effects or as an act of bravado. We report a series where two of eight men belonging to the same military unit experienced seizures after all eight ingested C4. **Case series:** A 19 y/o male (Patient A) with no medical problems or routine medications presented to an emergency department (ED) after several friends (including Patient B) witnessed him seizing and projectile vomiting at dinner. Shortly after arrival he had a second seizure, was noted to have frequent episodes of bigeminy and trigeminy, and was bradycardic at 40–50 bpm. He was treated with intravenous lorazepam, morphine and promethazine and admitted to the ICU. Initial laboratories were normal with the exception of his lactate (19.8 mmol/L) and bicarbonate (9.8 mmol/L), which spontaneously normalized within a few hours. Patient B, also 19 y/o with no past medical history or routine medications, had a witnessed tonic-clonic seizure lasting 45 seconds in the ED while visiting his friend (Patient A). This patient also had vomiting but more strikingly dislocated both of his shoulders during the witnessed seizure. The patient admitted he and several other members of his unit, including Patient A, each ingested pea-sized amounts of C4 approximately 4 hours prior to Patient A's seizure activity. He recalled feeling dizzy, nauseated, having blurred vision and vomiting at least three times about 2 hours after ingesting the C4. Both were discharged within 3 days with no lasting effects. **Conclusion:** These cases reinforce the need to better educate military service members that consumption of C4 is not a benign process and that acts of bravado by its ingestion can have harmful effects to the individual and unit involved. **Reference:** 1. Davies J, Roberts D, Hittridge A, et al. Oral C-4 plastic explosive in humans - a case series. *Clin Toxicol (Phila)* 2007; 45:454–7.

### 295. Does Washing-Up Liquid Cause Serious Eye Damage?

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**Objective:** According to the European Regulation on Classification, Labelling and Packaging of substances

and mixtures (EG 1272/2008), washing-up liquids must be labelled "Causes serious eye damage". The purpose of this study was to see if this labelling is consistent with the actual risk to the eyes. No retrospective study concerning this topic has been published before. **Methods:** All calls to the Swedish Poisons Information Centre concerning eye exposures to washing-up liquids between the 1st of January and the 31st of October 2011 were included. The cases were followed up by telephone interviews. Severity of symptoms was graded according to the Poisoning Severity Score (PSS).<sup>1</sup> **Results:** In total 163 cases were included and 84 (52%) could be followed up. Of those interviewed, 50% were exposed to concentrated washing-up liquid and 50% to diluted or unknown concentration. The symptoms were graded as minor (PSS 1) in 79 patients and moderate (PSS 2) in one. Four patients had no symptoms. No severe eye damage was seen. Only one patient, in the case graded as moderate, was examined by a doctor. Of the 42 patients exposed to concentrated washing-up liquid, 19 had symptoms for less than twelve hours, out of which 13 were asymptomatic within four hours. Twenty-one persons experienced prolonged discomfort between 12 hours and a few days. Of the 42 patients exposed to diluted or unknown concentration, 22 were asymptomatic within four hours, 34 within 12 hours and six had symptoms lasting longer than 12 hours. **Conclusion:** In the majority of cases the symptoms were classified as minor (PSS 1). About one fourth, in particular patients exposed to concentrated product, experienced prolonged discomfort, however only one patient sought medical care. No severe eye damage was recorded. In all exposures graded as minor the symptoms resolved spontaneously. In conclusion, this study shows that the labelling of washing-up liquids, "Causes serious eye damage" is inconsistent. **Reference:** 1. Persson HE, Sjöberg GK, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. *J Toxicol Clin Toxicol* 1998; 36:205–13.

**296. Stomach Perforation Following Liquid Nitrogen Ingestion Treated by Simultaneous Laparotomy and Intraoperative Endoscopy**  
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**Objective:** Liquid nitrogen is frequently used in industry, medicine and gastronomy. It boils at -196°C and rapidly evaporates when in contact with body temperature. Liquid nitrogen causes damage by two mechanisms: rapid freezing injury upon mucosal contact and rapid volume expansion by up to 700 times as nitrogen gas is formed, which can result in a tiny stomach perforation difficult to find during surgery. We report the case of stomach perforation after liquid nitrogen ingestion treated with an innovative combination of surgery and endoscopy. **Case report:** A 21-year old student drunk 2 dcl of distilled alcohol mixed with an unknown volume of liquid nitrogen prepared by friends at a student party in the university laboratory, since liquid nitrogen produces a white mist during eructation. Immediately afterwards, he felt distension in the upper abdomen that was followed by a sharp pain. At the Emergency Department 20 minutes later he had severe abdominal pain and dyspnea. On physical examination tachypnea and abdominal distension without peristaltic sounds were found. Abdominal X-ray showed a large amount of peritoneal gas. Computed tomography (CT) imaging of the abdomen and

thorax confirmed intra-peritoneal air with a normal mediastinum. Urgent laparotomy revealed a large amount of peritoneal gas and subperitoneal emphysema and hematoma of lesser stomach curvature, but without evident stomach or esophageal perforation. Subsequently the abdominal cavity was filled with saline solution and the stomach inflated with air during intra-operative esophagogastroscopy. In the esophagus endoscopy did not reveal any cold-induced lesion. Stomach was filled with previously ingested food, which obscured the view of endoscopist, but part of the perforation was identified immediately under the cardia. In the abdominal cavity lining air bubbles were observed leading to the stomach perforation extending from the gastric cardia to the pylorus covered by intact stomach peritoneum. Necrectomy of the lesser stomach curvature perforation was performed and the defect closed with interrupted sutures. Afterwards the patient was treated with parenteral hydration, antibiotics, antiemetic, analgesic and a proton pump inhibitor. The patient was discharged after one week. **Conclusion:** Liquid nitrogen ingestion can result in hidden stomach perforation with pneumoperitoneum that requires urgent laparotomy coupled by intra-operative gastroscopy.

**297. Sodium Azide Ingestion Associated with QRS Prolongation**

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**Objective:** To describe a case of intentional sodium azide ingestion associated with an atypical finding-QRS prolongation. **Case report:** A 28 YO laboratory technician intentionally ingested approximately 100 mg of sodium azide in an experiment to determine how much poison he could ingest to maximize self-harm without vomiting. He immediately felt shaky and sweaty. Public safety officers noted his distress and escorted him to the nearest emergency room (ED). He was evaluated within 20 minutes of the ingestion. Vital signs on arrival were: BP 85/38, HR 92, RR 15, SaO<sub>2</sub> 100%, T 36.3. He was tremulous and appeared ill, but had normal mentation and was not cyanotic. A nasogastric tube was placed and gastric contents aspirated. The aspirated material was placed in biohazard bags and discarded by environmental safety officers. He received 4L of isotonic saline in the ED with eventual resolution of his hypotension. The initial EKG shortly after arrival noted a QRS of 118 ms. He received two, 50 mL ampules of 8.4% sodium bicarbonate via IV bolus and repeat EKG 40 min later noted narrowing of the QRS to 104 ms. He was placed on a sodium bicarbonate drip at 150 mL/hr (3 amps in 1 L of D5W). Notable ED labs included a lactate of 5.3 mmol/L, potassium 2.8 mmol/L, glucose 147 mg/dL, and HCO<sub>3</sub> 20 mmol/L. Serum lithium concentration was 1.21 mmol/L (therapeutic reference range 0.5–1.5 mmol/L). Urine drug screen was negative for opiates, cocaine, amphetamines, cannabinoids, benzodiazepines and barbiturates. Serum ethanol, salicylate and acetaminophen concentrations were undetectable. He was admitted to a negative pressure room in the intensive care unit (ICU). The bicarbonate drip was stopped after 14 hours and repeat EKGs demonstrated QRS duration consistently < 100 ms. He had transient bradycardia during rest over the next two days but was discharged from the hospital 4 days later without sequelae. **Conclusion:** We describe a case of sodium bicarbonate-responsive QRS prolongation in a survivor of sodium azide poisoning.

**298. Experimental Production of Carbon Monoxide from Wood Pellets**

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**Objective:** It has been shown that fresh wood pellets used as biomass fuel for house heating systems emit volatile substances including carbon monoxide (CO).<sup>1</sup> Fatal CO poisoning has been reported in large pellet containers such as on overseas vessels.<sup>2</sup> After a case of fatal CO poisoning in a tenement pellet container we conducted experiments aimed to determine the amount of CO produced, and the influence of relative humidity and the type of pellets. **Methods:** Fresh EN 14961–2 class A1 and A2 quality wood pellets taken directly from production at two different manufacturers were stored in identical 60 litre air-tight polyethylene barrels (30 kg/barrel). Five aliquots each from pure spruce wood and spruce with high bark content were used, with different humidity (water added 0%, 1%, 2%, 3%, 4% of wood weight). The barrels were stored for 16 days at 26°C ambient temperature, after which relative humidity, CO and O<sub>2</sub> concentrations were measured in the headspace using Ecom-J2KN test systems. **Results:** Adding water to the pellets led to increasing relative humidity within the barrels (27% to 59%). Temperature in all barrels was stable at 26.7°C. CO content of headspace ranged from 3600 to 4400 ppm and from 3100 to 4800 ppm for the pure spruce and spruce/bark pellets respectively. The corresponding O<sub>2</sub> concentrations were 9.3% to 11.5% and 7.0% to 10.7% respectively. There was no correlation between relative humidity in the containers and the extent of CO emission, although there was a trend towards lower CO emission in higher relative humidity. There was no difference between the two pellet qualities. **Conclusion:** We showed that even small quantities of freshly produced wood pellets emit CO leading to life-threatening concentrations in non-ventilated containers. The production of gases including CO is associated with oxygen depletion with a negative correlation between CO emission and O<sub>2</sub> concentrations. Wood storage containers should be well ventilated, be equipped with a CO detector, and carry a label warning of CO poisoning. **References:** 1. Kuang X, Shankar TJ, Bi XT, et al. Characterization and kinetics study of off-gas emissions from stored wood pellets. *Ann Occup Hyg* 2008; 52:675–83. 2. Svedberg U, Samuelsson J, Melin S. Hazardous off-gassing of carbon monoxide and oxygen depletion during ocean transportation of wood pellets. *Ann Occup Hyg* 2008; 52:259–66.

**299. Human Exposure to Chemiluminescent Glow-Sticks: A Case Series from the French Poison and Toxicovigilance Centres**

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**Objective:** Glow-sticks are plastic rods that glow in the dark. Technically, they consist of two parts mixed

before use. They recently became a fashionable accessory used for decorative purposes in night clubs and parties, as well as for short-lived jewelry. Very few case descriptions and/or risk assessment of human exposure to glow-sticks are available, whereas in France the recent report of a cluster of intoxications raised interest for their possible harmful effect. We thus report a series of cases from the French Poison and Toxicovigilance centres (PTCs), and an assessment of the dangers and risks associated with these devices. *Methods:* All cases of glow-stick exposure reported to the French PTCs, from 1999 to 2010, were retrospectively analyzed. A search was conducted on the composition of commercial preparations through the PTCs' product composition database. Immediate and long-term risks were eventually evaluated, based on toxicological literature. *Results:* During the study period, 2979 exposure cases were reported to the French PTCs, with the number of reports increasing sharply since 2005. Because of the ways in which glow-sticks are used, accidental exposures were mainly observed at night (> 75%), during weekends (> 50%) and in summer, or between Christmas and the New Year (> 60%). Most cases of exposure involved children aged 1 to 9 years (87%). The majority (2524 cases) resulted from ingestion of glow-stick contents. However eye and/or skin contamination was also frequently reported. Irrespective of the exposure route, the immediate symptoms always resulted from irritation and were benign. Although their toxic properties are largely unknown, most components have irritant properties. They may also contain reprotoxic phthalates. The chemiluminescent dyes are mostly polycyclic aromatic hydrocarbons (PAH) whose chemical structure and "activation" during the chemiluminescent process indicate possible risks of genotoxicity and carcinogenicity. *Conclusion:* Glow-sticks are responsible for a rapidly growing number of accidental exposures. The immediate effects of these accidents are always benign. However, glow-sticks may contain compounds with toxic properties of concern (especially mutagenicity, carcinogenicity and/or reprotoxicity). Regulations should ensure that glow-stick composition is restricted to components with a demonstrated lack of toxic properties.

### 300. Accidental Exposures to Liquid Detergent Capsules

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*Objective:* Since last year Milan Poison Control Center has received a considerably increased number of toxicological enquiries about accidental exposures to washing machine liquid detergent capsules. Each capsule contains 30–35 mL of concentrated liquid laundry detergent, defined by a water soluble membrane that easily dissolves with moisture, mainly saliva or moist hands. The transparency of packaging, the bright colour and the softness of these liquid capsules makes them more attractive to children who become accidentally involved because they look like sweet bonbons or toys. This study aims to determine if this new formulation of washing machine laundry detergent involves a change of risk in this category, especially for young children. *Methods:* Between August 1st 2010 and October 31st 2011 the

Milan Poison Control Center collected 578 telephone enquiries relating to liquid detergent capsules. Every case was followed by a recall to submit a questionnaire about storage habits. *Results:* The majority of enquiries (N = 474; 81%) concerned children under 4 years of age. Exposure to these chemical products occurred mainly as a result of ingestion alone (N = 376; 65.1%), with eye contact alone (N = 36; 6.2%), cutaneous (N = 5; 0.9%) and multiple routes of exposure (N = 78; 13.5%). Most patients were symptomatic (N = 441; 72.3%), with vomiting (N = 308; 69.8%), coughing (n = 72; 16.3%), laryngospasm (N = 3; 0.7%), ocular hyperaemia (N = 70; 15.9%), corneal lesion (N = 8; 1.8), skin irritation (N = 32; 7.2%). *Conclusion:* This study suggests there is an increased risk of toxicity for capsule formulation compared to traditional washing machine laundry detergents. A comparison of symptomatic patients exposed to washing machine laundry detergents showed an increased risk for the capsule formulation: patients exposed to traditional washing machine laundry detergents were symptomatic in 27% of cases while patients exposed to capsules were symptomatic in 76% cases. The study showed that severity of symptoms with capsule formulation requires an increased time of hospitalization. After the market entry of the capsule formulation enquiries to the Milan Poison Control Center regarding washing machine laundry detergents have doubled due to their very attractive appearance for children.

### 301. Organic Mercury Poisoning. A Thing of the Past? A Case Report

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<sup>1</sup>GIZ-Nord Poisons Centre, University Medical Center, Göttingen; <sup>2</sup>BDH-Klinik, Hessisch Oldendorf, Germany

*Objective:* Nowadays, life-threatening heavy metal poisonings are rare in developed countries. This case report may raise the awareness of these very infrequent intoxications. *Case report:* In July 2011 a 40 year old male consulted his general practitioner with abnormal fatigue and fever. The doctor prescribed an antibiotic whereon the patient developed skin alterations which were interpreted as drug eruption. The following week the symptoms progressed and body temperature rose continuously. Due to a steady decrease of the patient's general condition he was transferred to a hospital. During hospitalisation he developed centripetal sensory disorders, beginning at palms and soles. In the following days a progressive paralysis and renal failure occurred and the patient was transferred to a university hospital. In the following weeks the patient's condition continued to deteriorate. The exanthema worsened, the fever was resistant to therapy, the patient became quadriplegic, lost consciousness and haemodialysis was necessary. He was treated under the putative diagnosis: "Guillain-Barre syndrome" with immunoglobulins, glucocorticoids and plasmapheresis without clinical improvement. Six weeks after the first symptoms the patient's serum was examined for mercury. It showed 2929 micrograms/L for mercury and 1538 micrograms/L for methyl mercury. Chelation therapy with 2,3-dimercapto-1-propanesulfonic acid (DMPS) was started. The mercury serum levels were reduced significantly albeit the clinical status did not improve. This could be due to the late onset of therapy. The cause of the mercury intake is unclear and under legal investigation. *Conclusion:* Hindsight is easier than foresight. While neurotoxicity, renal dysfunction and dermatitis are hallmarks of poisonings

with organic mercury, this differential diagnosis is often not taken into consideration because of the rareness of this intoxication today.

### 302. Thirty-Six Hours of Elevated Carboxyhemoglobin Concentrations Following Methylene Chloride Exposure: To Dive or Not to Dive?

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*Objective:* Carbon monoxide (CO) generation is a known complication of methylene chloride (MeCl) exposure. We report a patient exposed to 36.5 hours of elevated carboxyhemoglobin (COHb) following MeCl exposure without neuro-psychiatric sequelae. We consider this in the context of similar cases treated with hyperbaric oxygen (HBO) due to concern for "soaking" in the setting of ongoing endogenous CO production. *Case report:* A 51 year-old man was found unresponsive in his car surrounded by rags and an empty bottle of paint stripper. ED vital signs: BP 160/70 mmHg; HR 118 beats/min; RR 14 breaths/min; SpO<sub>2</sub> 100% RA. VBG on supplemental oxygen: pH 7.4; PCO<sub>2</sub> 5.2 kPa; PO<sub>2</sub> 13.3 kPa. He was intubated and placed on 100% O<sub>2</sub>. The paint thinner label revealed components: MeCl 90%; methanol 7%; toluene 2%. COHb one hour after arrival was 3.9%. Serial concentrations revealed a rising CO that reached 7% by 5.5 hours, 8% by 10.7 hours, and peaked at 12.1%, 18.2 hours after presentation, before falling to 3.6% at 36.5 hours. He was extubated 36 hours after arrival and remained neurologically intact until discharge. Telephone follow up was performed one month later and he was well and without complaints. *Conclusion:* In acute CO poisoning loss of consciousness and a long time span of exposure ("soaking") are risk factors for neuropsychiatric sequelae.<sup>1</sup> In cases of acute CO poisoning, evidence suggests that HBO prevents development of these cognitive deficits.<sup>2</sup> While HBO has also been used to treat CO poisoning following MeCl exposure with similar COHb peaks (11%, 13%),<sup>3</sup> there is no prospective evaluation of the role of HBO. CO poisoning following MeCl exposure can cause neuropsychiatric sequelae.<sup>3</sup> While HBO may be considered in such cases due to a concern for prolonged exposure due to continuous endogenous CO production, patients may recover fully with only 100% O<sub>2</sub>. *References:* 1. Hardy KR, Thom SR. Pathophysiology and treatment of carbon monoxide poisoning. *J Toxicol Clin Toxicol* 1994; 32:613–29. 2. Weaver LK, Hopkins RO, Chan KJ, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med* 2002; 347:1057–67. 3. Rioux JP, Myers RA. Hyperbaric oxygen for methylene chloride poisoning: report on two cases. *Ann Emerg Med* 1989; 18:691–95.

### 303. Caustic Ingestion: An 11-Year Retrospective Analysis of 190 Patients

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*Objective:* Caustic gastrointestinal (GI) lesions are one of the most devastating events in acute toxicology, often asso-

ciated with high mortality risk and permanent sequelae.<sup>1</sup> Caustics can be divided into acids and alkalis according to their pH. The objective of this review is to evaluate the different epidemiology, outcome and mortality rate based on different pH of caustic substances. *Methods:* We observed 190 consecutive cases of caustic ingestion admitted to our unit from 1999 to 2010. Epidemiology, degree of oral and endoscopic gastrointestinal (GI) tract lesions and mortality rate were examined and evaluated both in the total sample and in consideration of the caustic pH (acid or alkali). *Results:* 190 (100%) consecutive cases were examined; 147 (77.4%) were alkali ingestions (32 strong alkalis) and 43 (22.6%) were acid ingestions (30 strong acids). There were 108 oral injuries (57%). One hundred and twenty-nine cases (68%) of the total sample underwent endoscopy. Endoscopic GI injuries were present in 95 (74%) cases; 18 (86%) and 77 (71%) in acid and alkalis ingestion, respectively. A correlation between oral and endoscopic GI lesions was analyzed and 26 (63%) patients without oral lesions showed esophageal and/or gastric lesions. Survival rate was 96.3% (183 cases) in the total sample while mortality rate was 3.7% (7 cases). Six of the 7 patients who died had a history of strong acid ingestion. In particular, mortality rate was 20% and 3.2% of strong acid and alkali ingestions, respectively. Cases discharged with GI sequelae were 4%, all alkali ingestions. All deceased patients had a history of self-harm ingestion. *Conclusion:* Voluntary strong acid ingestion showed a higher mortality rate than strong alkali ingestion. Alkali ingestion was characterized by GI sequelae. Following the clinical relevance of caustic ingestions, an emergency treatment algorithm is needed, in order to better treat caustic ingestions. *Reference:* 1. Bronstein AC, Spyker DA, Cantilena LR Jr, et al. 2009 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 27th Annual Report. *Clin Toxicol (Phila)* 2010; 48:979–1178.

### 304. Deafness after Barium Chloride Poisoning: A Case Report

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*Objective:* We report a rare case of barium chloride poisoning following suicidal oral ingestion. *Case report:* A female patient (32 years, 55 kg) was assigned to the intensive care unit (ICU) 6 hours after ingestion of an unidentified white crystalline powder. Subsequently the substance was identified as barium chloride. Clinical examination showed signs of circulatory shock. Neurological symptoms included quadriplegia and unintended urination. Blood examinations revealed metabolic acidosis, acute kidney failure and a lowered potassium level at 1.8 mmol/L. Primary decontamination was attempted by oral treatment with sodium sulfate and secondary decontamination by hemodialysis. Serum levels of barium were highly elevated (60 mg/L). Within the first day the patient developed biauricular deafness which persisted until discharge from the ICU. Treatment with hemodialysis and normalization of potassium levels lead to complete remission of the paralysis. Deafness remains and 6 months later the patient received a one-side cochlea implant. *Conclusion:* Intoxications following oral ingestion of barium chloride were rarely reported during recent decades. As a consequence the knowledge of the pathophysiology and treatment is limited.<sup>1–4</sup> Toxic effects of barium chloride most likely result from the blockage of cellular potassium channels leading to a permanent depolarization of nerve and muscle cells. Arrhythmia, paralysis and seizures are

common clinical manifestations.<sup>5</sup> Distribution and accumulation in bones and other tissues limit enhanced elimination to a short time window. This leads to the necessity for an aggressive decontamination strategy including oral treatment with sodium sulfate, hemodialysis and substitution of potassium. *References:* 1. Fogliani J, Giraud E, Henriquet D, et al. [Voluntary barium poisoning]. [Article in French]. *Ann Fr Anesth Reanim* 1993; 12:508–11. 2. Jourdan S, Bertoni M, Sergio P, et al. Suicidal poisoning with barium chloride. *Forensic Sci Int* 2001; 119:263–5. 3. Picheta S, Kłopotowski T, Kicka M, et al. [Acute poisoning due to barium chloride—case report]. [Article in Polish]. *Prz Lek* 2010; 67:633–5. 4. Fiedorowicz-Fabrycy I, Gruner-Zarnoch E, Smulski H, et al. [A case of suicidal poisoning with barium chloride - BaCl<sub>2</sub> (author's transl)]. [Article in Polish]. *Prz Lek* 1975; 32:302–4. 5. Roza O, Berman LB. The pathophysiology of barium: hypokalemic and cardiovascular effects. *J Pharmacol Exp Ther* 1971; 177:433–9.

### 305. A Silly Way to Die: Use of N-Acetylcysteine in Hydrocarbon Ingestion

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*Background:* Most of the compounds known as hydrocarbons are derivatives of petroleum distillation. Their toxicity is caused by aliphatic and aromatic and also halogenated hydrocarbons. Petroleum and pine trees are the two primary sources for most liquid and solid aliphatic hydrocarbons. Inhalation of any volatile hydrocarbon sensitizes the heart to the endogenous catecholamines, lowering the threshold for ventricular fibrillation. *Case series:* The authors present a series of 5 cases ingestion of hydrocarbons for suicidal purpose treated with supportive therapy, N-acetylcysteine (NAC) and intravenous fat emulsion (IFE). In this series of cases we have treated 5 patients (1 male and 4 female) aged between 35 and 58 years, who came to our emergency department after voluntary ingestion of compounds containing hydrocarbons such as stain removers, solvents, craft supplies, trichlorethylene. All patients came to our attention about one hour after ingestion of hydrocarbons. All were stuporous or comatose with a Glasgow Coma Scale average of 8 (minimum 5, maximum 11). All patients underwent endotracheal intubation, supportive care and monitoring of liver, renal and coagulation function. In all cases an ECG was performed as well as an analysis of blood gas exchange. Hepatotoxicity was defined as peak serum aminotransferases > 1000 IU/L and in 4 cases administration of intravenous NAC was started. One female patient showed ventricular tachycardia, requiring two boluses of 100 mL of IFE followed by an infusion at 0.25 micrograms/kg/min and stabilized over the next 3 hours. All patients underwent a gradual improvement in gas exchange and the state of consciousness; blood coagulation parameters also gradually improved. Treatment with N-acetylcysteine was continued for 3 days, with return to normal liver function. *Conclusion:* Ingestion of hydrocarbons is an unusual event. Although the etiopathogenesis is not yet fully understood, the toxicity affects several sites including the respiratory system, central and peripheral nervous system, gastrointestinal, liver, skin and mucous membranes. The early use of NAC, although “off label”, has been suggested on the basis of the finding of important coagulation disorders, and hepatotoxicity. We hypothesize that early and prolonged use may have contributed to the improvement of liver functionality and the prevention of further damage.

### 306. Acute Inhaled Xylene Poisoning Confirmed by Methyl Hippuric Acid Urine Test

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*Objective:* To report a case of acute poisoning from xylene inhalation confirmed by determination of urinary methyl hippuric acid (MHA). *Case report:* Two young healthy adults aged 21–23 years were brought to the emergency department after being found unconscious at home. Partial improvement was noted by the paramedics en-route to the hospital. According to the family, they had painted a closed room before collapsing, using unknown paint and thinner. On admission, they were confused and agitated, with pulse rate of 90–110/minute, blood pressure 120/78–142/80 mmHg, respiratory rate 20/minute, oxygen saturation 95–100% (room air), and mydriasis. Electrocardiograms and chest x-rays were interpreted as normal. Complete blood count, kidney and liver functions were within normal range. MHA, a metabolite of xylene used in occupational biomonitoring, was measured in the patients' urine by HPLC with UV detector. The levels determined were 2.57–2.68 g/g creatinine (Biological Exposure Indices (BEI) 0–1.5 g/g creatinine). Levels of urinary hippuric acid, a toluene metabolite, were within normal range (0.18–0.46 g/g creatinine, BEI 0–2.5 g/g creatinine). In the cardiac intensive care unit, where they were admitted for observation, the respiratory and hemodynamic parameters were within normal limits and stable. Confusion and agitation were replaced by drowsiness. Eventually they regained full consciousness. Physical examination 24 hours after admission was unremarkable. Continuous cardiac monitoring and repeated electrocardiograms did not reveal cardiac arrhythmias. One patient developed mild elevation of alanine aminotransferase (80 U/L) and aspartate aminotransferase (71 U/L), which returned to normal within 24 hours. The patients were discharged after 48 hours' observation without any sequelae. *Conclusion:* Acute xylene inhalation was confirmed in our patients by the presence of MHA in their urine. The exposure resulted in neurological symptoms and mild hepatic injury. The assay of urinary MHA has no known interferences and is considered specific. Two reports on acute inhaled xylene poisoning involving six workers were published.<sup>1,2</sup> Xylene was co-inhaled with toluene and their metabolites were not measured. To our knowledge, this is the first report of acute xylene poisoning following inhalation that was confirmed by urinary MHA. It is suggested that urinary MHA be determined whenever confirmation of acute exposure to xylene is required. *References:* 1. Moreley R, Eccleston DW, Douglas CP, et al. Xylene poisoning: A report on one fatal case and two cases of recovery after prolonged unconsciousness. *BMJ* 1970; 3:442–3. 2. Glaser J, Dessauer M, Proksch E. Acute polyneuropathy caused by inhalation of solvent mixtures in varnish removers and thinners in normal commercial use. *Dtsch Med Wochenschr* 1985; 110:1374–7. [Article in German, Abstract in English].

### 307. CS Tear Gas Exposure: Prevention and Decontamination with Amphoteric, Chelating and Hypertonic Solution

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*Objective:* Chlorobenzylidene-malononitrile (CS) is the tear gas most commonly used by the police. CS interacts with muco-cutaneous sensory nerve receptors and causes

severe facial pain with reflex blepharospasm and lacrimation. The aim of this study was to evaluate an amphoteric, chelating and hypertonic decontamination solution in CS exposure. **Methods:** 22 police officers were divided into three groups. The first (CS) group of 6 was exposed to CS only. The second (pre-exposure) group of 8 sprayed their faces with the amphoteric and chelating solution just before CS exposure. The third (post-exposure) group of 8 sprayed their faces with the amphoteric and chelating solution immediately after CS exposure. The CS exposure was achieved by running for 20 seconds through a CS cloud prepared with 8 CS hand grenades during regular police training. The time between exiting CS and arriving at the "ready for action" checkpoint established by themselves was measured. Their facial pain both inside the CS cloud and at the checkpoint was assessed by the pain rating scale (1–10 points). Data are presented as mean  $\pm$  SD, using the one-way between groups ANOVA and Bonferroni correction method. **Results:** Analyses of the differences in pain and time between different groups revealed a significant difference. The *post hoc* test results showed that the pain level inside the CS cloud was significantly lower in the pre-exposed group ( $5.6 \pm 1.1$ ) than in the CS group ( $9.7 \pm 0.5$ ) and in the post-exposure group ( $9.1 \pm 0.4$ ). The time interval between CS exposure and arrival at the checkpoint in the pre-exposure group ( $1:26 \pm 0:44$  min) was significantly shorter than both in the CS group ( $2:28 \pm 0:25$  min) and post-exposure group ( $2:30 \pm 0:48$  min). The residual pain at the checkpoint in the pre-exposure ( $1.1 \pm 0.4$ ) and post-exposure ( $1.4 \pm 0.7$ ) groups was similar with a significant lower pain level than in the CS group ( $2.3 \pm 0.5$ ). **Conclusion:** CS exposure results in severe facial pain putting policemen out of action for three minutes. CS decontamination with the amphoteric and chelating solution reduces facial pain, while prevention with it reduces pain and recovery time.

### 308. Alveolar Hemorrhagic Syndrome Secondary to Illegal Subcutaneous Injection of Industrial Liquid Polydimethylsiloxane for Cosmetic Purposes

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**Objective:** To report a case of pulmonary hemorrhage after multiple subcutaneous injections of industrial liquid silicone. **Case report:** A 24-year-old male was seen at the Emergency Department complaining of dyspnea and fever for the previous 2 days. He had injected an unknown quantity of industrial liquid silicone subcutaneously into his buttocks 10 days earlier. He presented with severe hypoxemia, being intubated and put on mechanical ventilation. Blood was seen in the oro-tracheal tube during intubation. Hemoglobin level was 6.5 g/dL. Thorax images showed a diffuse and bilateral ground glass pattern suggesting alveolar filling. Lung hemorrhage was then taken as probable diagnosis. Pulse therapy with methylprednisolone was then given for 3 days with good improvement of the ventilatory parameters and recovery of hemoglobin levels. No blood transfusion was necessary. After two weeks he was doing fine with small residual images in both lungs and SpO<sub>2</sub> = 95%. **Conclusion:** Silicone syndrome is produced by migration of liquid silicone (polydimethylsiloxane) into the pulmonary capillaries after subcutaneous injection, resulting in nonthrombotic pulmonary emboli. Four histological patterns have been described in that situation: the mere presence of silicone emboli; acute pneumonitis; congestion and alveolar hemorrhage; and diffuse alveolar

hemorrhage.<sup>1</sup> Symptoms generally appear 72 hours after the injection consisting of fever, tachycardia, cough, dyspnea, haemoptysis, and chest pain. Petechiae, hypoxemia and loss of consciousness can follow. The clinical findings are very similar to that of fat embolism. The mechanism of hemorrhage indicates probably a role for the coagulation system.<sup>2</sup> Another tentative explanation is that the ingestion of the silicone by alveolar macrophages may induce an inflammatory response increasing vascular permeability, activating endothelial cells, and modulating local immunoregulatory responses.<sup>1</sup> Treatment consists of lung ventilation, and corticosteroids, although no scientific evidence supports its obligatory use. Fatalities are related to cerebral hypoxia. **References:** 1. Parikh R, Karim K, Parikh N, et al. Acute pneumonitis and alveolar hemorrhage after subcutaneous injection of liquid silicone. *Ann Clin Lab Sci* 2008; 38:380–5. 2. Schmid A, Tzur A, Leshko L, et al. Silicone embolism syndrome: a case report, review of the literature, and comparison with fat embolism syndrome. *Chest* 2005; 127:2276–81.

### 309. Is There Any Relationship between Organophosphate Poisoning and Cardiac Injury?

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**Objective:** Organophosphates are insecticides which are widely used as suicidal agents in Iran. They are associated with different types of cardiac complications including cardiac arrest and arrhythmia, however their role in cardiac injury is not yet known. The aim of this study was to investigate whether or not myocardial damage occurs in patients with cholinesterase poisoning. **Methods:** It was a prospective study conducted from January 2008 to March 2010. Cohorts of patients with cholinesterase poisoning due to suicidal attempts who have been referred to Loghman hospital were selected. Patients who had taken more than one poison or were using concomitant drugs were excluded. Physical examination was performed on admission to discover warning signs. Peripheral arterial blood gases, complete blood count, creatine kinase (CK), creatine kinase-myocardial band (CK-MB), troponin-T measurements were performed in all cases. **Results:** There were 24 patients, 7 of them women, with the mean age of  $41.2 \pm 15.05$  who were included in this study. Non-survivors had significantly higher levels of systolic blood pressure, PaO<sub>2</sub>, PCO<sub>2</sub>, HCO<sub>3</sub>, Glasgow Coma Scale scoring and longer duration of mechanical ventilation. Serum markers of cardiac injury were significantly higher in non-survivors in comparison with surviving patients. **Conclusion:** We have shown increased serum markers of cardiac injury as a predictive factor of death in patients with organophosphate poisoning.

### 310. Hepatic Encephalopathy and Death Following Zinc Phosphide Poisoning

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**Objective:** Zinc phosphide is a commonly used rodenticide in developing countries including India and Iran<sup>1</sup>. When exposed to moisture, or gastric juice

hydrochloride, it liberates highly lethal phosphine gas. **Case report:** We present a 21-year old man who attempted suicide by ingestion of 4 teaspoons (20–30 g) of a black powder with a garlic smell labelled as zinc phosphide. The patient was brought to the hospital 45 minutes after ingestion. At presentation he was alert, oriented, haemodynamically stable, complaining of nausea, vomiting and abdominal pain. Gastric washing was performed and charcoal and sorbitol was given. Twelve hours later abdominal radiography showed radio-opacity in right lower quadrant. Further toxicology tests of the ingested powder and stomach fluid confirmed zinc phosphide poisoning. The patient was monitored carefully for any signs and symptoms of toxicity. Initial diagnostic testing consisting of a complete blood count, serum chemistry profile, and arterial blood gas (ABG) analysis, liver and kidney function test which were all in normal range. On day 2 he had mild abdominal pain. In spite of receiving repeated doses of charcoal and sorbitol the patient did not have defecation. On day 3 whole bowel irrigation with polyethylene glycol treatment was performed. On day 4 the patient became very agitated, and lethargic. ABG showed severe metabolic acidosis (pH: 7.1, serum bicarbonate: 6.0 mmol/L) and deranged liver function and clotting tests (PT > 25 sec, INR: 4.1). The patient was immediately intubated, received intravenous (IV) sodium bicarbonate, magnesium sulfate and vitamin K. The patient became icteric (bilirubin total: 15.3 and direct: 6.4 mg/dL) and developed hepatic encephalopathy. On day 5 he became hypotensive, hypoglycemic and oliguric resistant to IV fluid therapy and vasopressor infusion. On the day 6 he developed bradycardia and cardiac arrest. Thirty minutes cardiopulmonary resuscitation was unsuccessful and he was pronounced dead. **Conclusion:** Zinc phosphide is a chemical used mainly as a rodenticide. Phosphine is the main cause of toxicity. The affected organs are cardiovascular, respiratory, gastrointestinal, hepatic and blood. **Reference:** 1. Moghadamnia AA, Abdollahi M. An epidemiological study of poisoning in northern Islamic Republic of Iran. *East Mediterr Health J* 2002; 8:88–94.

### 311. Acute Deliberate Organophosphate (Coumaphos) Poisoning with Intermediate Syndrome in a One Year Old Child

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**Objective:** To report a case of acute organophosphate poisoning in a one year old child and development of intermediate syndrome in just eight hours after exposure. **Case report:** A case of a previously well one year old child who came to the emergency room because of sudden onset of difficulty of breathing, cyanosis, excessive oral secretions, one episode of diarrhea and weakness noted three hours earlier after ingesting allegedly contaminated powdered milk formula. Vital signs showed a blood pressure of 90/60, cardiac rate of 112 per minute, respiratory rate of 12 cycles per minute and axillary temperature of 35.4 degrees Celsius. Arterial blood gas analysis showed respiratory acidosis. Endotracheal intubation was immediately carried out and was hooked on mechanical ventilation. The toxidrome of the patient was compatible with acute cholinergic excess; hence a trial dose of atropine was given with some improvement. Eight hours later, neurological examination showed absence of deep tendon reflexes, no spontaneous respiration, no response to pain, flaccid muscle tone, no neck rigidity and lateralizing signs but with spontaneous eye opening. Red blood cell (RBC) cholinesterase

determination showed a result of 0.057 delta pH/hr, which is significantly depressed. Atropine was given at 0.02 mg/kg intravenously until full atropinization was achieved. Packed RBC transfusion was given. Twenty-four hours later, the patient was noted to have response to painful stimuli and spontaneous respiration. A repeat RBC cholinesterase determination showed a result of 0.25 delta pH/hr. Atropine was continued as needed. Test was done on the allegedly contaminated milk using GC-MS; it was positive for coumaphos. The patient was discharged after seven days. **Conclusion:** Intermediate syndrome usually develops within 48–96 hours after acute cholinergic crisis due to prolonged inhibition of cholinesterases.

### 312. Withdrawn

### 313. Occupational Carbamate Poisoning

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**Objective:** Carbamate insecticide is well absorbed via the gastrointestinal tract, skin and respiratory tract. Exposure to and poisoning by carbamates is now one of the major poisonings in Thailand. The objective was to study the clinical manifestation and severity of carbamate poisoning in occupational dermal and inhalation exposure. **Methods:** This was a retrospective study. All cases of pure carbamate occupational exposure and poisoning from Ramathibodi Poison Center Toxic Exposure Surveillance system from 2005–2010 were included. Demographic data, clinical manifestations and severity were analyzed. **Results:** During these 6 years, a total of 3,183 cases were included. Methomyl accounted for 48.7%, carbofuran 25.2% and others 26.9%. Among these, 170 cases were identified as occupational exposure. Ninety-six cases (56.47%) were poisoned by carbofuran, 35 cases (20.59%) were by methomyl and 39 cases (22.94%) by other carbamates. Carbofuran is 3% grain and applied by sowing, but methomyl is a soluble concentrate or water soluble powder and applied by spraying the solution. Most of the patients did not use personal protective equipment (PPE) nor properly handled the insecticide to protect themselves. Clinical manifestations of occupational carbofuran poisoning included nausea/vomiting (82.29%), headache (56.25%) and miosis (19.79%). Diarrhea, bradycardia and hypersalivation were less commonly found. For methomyl poisoning, nausea/vomiting (74.29%), headache (57.14%) and palpitations (11.43%) were the common manifestation. The median onset of poisoning was 3.5 hours (30 minutes–36 hours) for carbofuran and 4.00 hours (10 minutes–72 hours) for methomyl. Medical outcomes of most cases were minimal severity. Only one case of each carbamate required mechanical ventilation for several hours, but no mortality was found in either chemical. **Conclusion:** Occupational exposures of carbamate poisoning were commonly mild and rarely accounted for serious poisoning. Most poisoning cases had a good outcome and rapid recovery. Inadequate PPE would be one of the major factors in occupational exposure and poisoning. Educating agriculturists about the good practice of pesticide application should be able to prevent and minimize occupational poisoning.

### 314. An Analysis of Paediatric Pesticide Poisoning at a Tertiary Children's Hospital in South Africa

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**Objective:** The paucity of data on childhood pesticide poisonings in developing countries precludes estimation of incidence.<sup>1,2</sup> In South Africa, the increasing use of pesticides<sup>2</sup> emphasises the need to quantify and describe paediatric incidents, and to compare these with other common groups of toxins to which children are exposed.<sup>3–5</sup> **Methods:** Cases were identified by review of the Red Cross War Memorial Children's Hospital (RCWMCH) records from 2003 to 2008. **Results:** There were 306 patients with 311 pesticide incidents, which increased annually from 30 incidents in 2003 to 69 in 2008. They represent 11% of all poisoning incidents (N = 2872) over the 6-year period. Although other toxin groups account for more incidents (drugs N = 988; paraffin (kerosene) N = 692), pesticide incidents represent 46% of fatalities (N = 6 of 13) and 54% of incidents with severe presentations (N = 91 of 167 with Poisoning Severity Score (PSS) 3). The largest groups of pesticides were cholinergics (includes organophosphates and carbamates), anticoagulants and unknowns (N = 203, 35 and 45). In 44 of the 311 pesticide incidents, the implicated pesticide had been purchased on the street; so-called illicit "street pesticides". When compared to presentations in 1987, pesticide incidents increased from 0.6% (N = 7) in 1987 to 15% (N = 69) in 2008. **Conclusion:** The rising number of childhood pesticide incidents, their associated morbidity and mortality and the occurrence of "street pesticides" require urgent attention. **References:** 1. United Nations: Childhood pesticide poisoning: Information for advocacy and action 2004. Available at <http://www.who.int/ceh/publications/pestipoin/en/>. [accessed Nov 2011]. 2. London L, Bailie R. Challenges for improving surveillance for pesticide poisoning: policy implications for developing countries. *Int J Epidemiol* 2001; 30:564–70. 3. Balme KH, Roberts JC, Glasstone M, et al. Pesticide poisonings at a tertiary children's hospital in South Africa: an increasing problem. *Clin Toxicol (Phila)* 2010; 48:928–34. 4. Balme KH, Roberts JC, Glasstone M, Curling L, Mann MD. The changing trends of childhood poisoning at a tertiary children's hospital in South Africa. *S Afr Med J* 2012; 102:142–6. 5. Roberts JC, Leary PM, Mann MD, et al. The pattern of childhood poisoning in the western Cape. *S Afr Med J* 1990; 78:22–4.

### 315. Use of Saliva as Biological Matrix for Diagnosis of Acute Pesticides Poisoning

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**Objective:** The use of saliva as biological matrix for toxicological analysis increased in the last decade, mainly for the determination of drugs and drug of abuse.<sup>1,2</sup> However, there are few references to the use of this matrix in emergency toxicology, or to detect pesticide poisonings.<sup>3</sup> The aim of this study was to evaluate the feasibility of saliva analysis for diagnosis of acute poisoning by pesticides. **Method:** 25 pesticides or their metabolites

(carbamates, organophosphates, and coumarin) were selected. The sample preparation was based on simple protein precipitation and dilution prior to injection into the chromatographic system. One hundred microliters of sample were transferred to a polypropylene tube, and 300 microliters of acetonitrile added (containing internal standard, BDMC 20 ng/mL). After agitation and centrifugation, 100 microliter of supernatant were transferred to a glass vial containing 900 microliter of ultrapure water and 10 microliter of this solution were injected into the LC-MS/MS system. Analyses were performed in multiple reaction monitoring (MRM) mode, with the identification by relative retention time and two MRM transitions ratio. The analytical method was fully validated before sample analysis, considering the parameters' detection limit, quantification limit, linearity, precision, accuracy, recovery and matrix effect. Saliva and plasma samples, collected from patients treated at the Campinas Poison Control Center were used for analysis. **Results:** From all investigated pesticides, we detected the presence of acephate, aldicarb, aldicarb-sulfoxide, aldicarb-sulfone, methomyl, carbofuran, 3-hydroxy-carbofuran, 3-keto-carbofuran at concentrations ranging from 5 ng/mL (limit of quantification) to 24.6 mg/mL. For some analytes, good correlation was observed ( $r > 0.90$ ) between salivary and plasma concentrations. **Conclusion:** The results demonstrate the usefulness of saliva for diagnosis of acute poisoning by pesticides. It should be noted that saliva is a less complex matrix than blood derivatives, its collection is non-invasive and provides good correlation with plasma levels. **References:** 1. Lilliusunde P. Analytical techniques for drug detection in oral fluid. *Ther Drug Monit* 2008; 30:181–187. 2. Pil K, Verstraete A. Current developments in drug testing in oral fluid. *Ther Drug Monit* 2008; 30:196–202. 3. Barr DB, Needham LL. Analytical methods for biological monitoring of exposure to pesticides: a review. *J Chromatogr B Analyt Technol Biomed Life Sci* 2002; 778:5–29.

### 316. Pesticide Enquiries to the National Poisons Information Centre of Ireland: A Prospective 4 Year Study

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**Objective:** To characterise the epidemiology of pesticide enquiries to the National Poisons Information Centre (NPIC) in Dublin. **Methods:** This study prospectively examined all cases involving pesticides reported to the NPIC from 1st May 2006 to 30th April 2010 inclusive. Information on enquiry source, pesticide agent, route of exposure and patient data were collated. **Results:** 1030 cases of pesticides were reported over 4 years. Twenty-eight per cent of enquiries originated from members of the public (MOPs), 27% from hospitals, 18% from General Practitioner (GP) surgeries, 15% from GP out-of-hours services, 8% from veterinary professionals and 4% from other sources. The majority of exposures occurred in a domestic setting (79%), 6.3% at work with others happening in open or unspecified areas. Enquiries related to herbicides (39.7%), rodenticides (28%), insecticides (17.5%), molluscicides (6%), unknown agents (3.2%), mixtures of pesticides (1.9%), fungicides (1.5%), with moss killers and repellents both at 1.1%. Eighty-one per cent of all cases were accidental; 7.4% were deliberate and the remainder unknown. The route of exposure was mainly oral (55.5%), followed by dermal (11%), inhalation (10%) and ocular exposures (4%). In 13% of cases multiple routes of exposure were reported. The remaining 6.5% calls were information

requests. The total number of human exposures was 904 (87%). Fifty-one per cent of cases involved children under 12 years. Males (61%) outnumbered females. Seventy per cent of all patients were symptomatic. A wide range of symptoms were reported with the most predominant being gastrointestinal disturbances (nausea, vomiting and diarrhoea). Other features that were reported in order of significance were skin effects (irritation and rash), general malaise, eye pain, sore throat and respiratory symptoms. Seven deaths (0.7%) were reported during the study period. Five of these were deliberate paraquat overdoses. **Conclusion:** The National Poisons Information Centre in Dublin received over a thousand pesticide related enquiries between 2006 and 2010. The most common symptoms were gastrointestinal disturbances followed by skin irritation. The majority of ingestions were accidental which reflects the low mortality rate reported.

### 317. Public Health Response Following Poisoning with Illegal Brodifacoum (0.5%) Rodenticide

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**Objective:** The long-acting anticoagulant rodenticide brodifacoum has been commercially available at a concentration of 0.005%. The sale of more concentrated formulations is illegal in many countries, but can be purchased on-line and from clandestine vendors. We report a case of severe coagulopathy with life-threatening hemorrhage following the ingestion of a small volume of highly concentrated 0.5% brodifacoum, and the resulting public health response. **Case report:** A 24 year-old woman presented to the emergency department (ED) with hematemesis, epistaxis, and gross hematuria 12 days after ingesting a 3 mL vial of a blue liquid that she mistook for an herbal cold preparation. The product, purchased from a street vendor in New York City's Chinatown, was labeled "The Cat Be Unemployed," containing 0.5% brodifacoum. Her vitals included BP 87/49 mmHg and pulse 94/min. Laboratory data: INR > 10, platelets 196 x 10<sup>3</sup>/μL, hemoglobin 7.2 g/dL, factor VII, 7% (day 3). Following treatment with 4 units fresh frozen plasma (FFP), 2 units packed red blood cells, 10 mg IV vitamin K, and 60 mg PO vitamin K every 6 hours (Q6H), her hemodynamic status stabilized. She was discharged on hospital day 4 on an outpatient regimen of vitamin K 75 mg po every 6 hours, which was gradually tapered to 25 mg Q6H. She required > 12 weeks of therapy due to prolonged coagulopathy. Regional and federal authorities were notified by the poison center, and an undercover investigation revealed numerous vendors of illegal rodenticides and pesticides in the Chinatown area. These efforts lead to the confiscation of thousands of illegal products and the prosecution of several vendors. **Conclusion:** Prolonged coagulopathy has been reported following massive ingestions of 0.005% brodifacoum. In this case, a single small-volume ingestion of 0.5% brodifacoum, a formulation 100 times more concentrated than commercially available rodenticides, resulted in life-threatening coagulopathy requiring extended outpatient treatment with high-dose vitamin K. The availability of such concentrated formulations, in a colorful blue solution that may be appealing to children, poses a great public health risk. This case illustrates how the poison center, acting as the identifier of a sentinel event, can work with appropriate authorities to spearhead the eradication of a grave public health threat.

### 318. Self-Poisoning by Injection of Dimethoate:

#### Case Report

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**Objective:** Dimethoate toxicity in humans is recorded after ingestion, inhalation and dermal absorption. This unique case of poisoning by intravenous/partially paravenous application of dimethoate is presented. **Case report:** A 56-year old man attempted suicide by injecting about 40–50 mL of insecticide containing 40% of dimethoate into the left cubital area. At admission reddening of the skin and bullous changes were noticed due to the injection and applied dose. Six to eight hours after the attempt, the patient was somnolent. Vital signs included a pulse of 120 beats/min, blood pressure 110/70 mmHg, and respiratory rate of 18 breaths/min. Pupils were miotic, lung auscultation revealed normal breath sounds. The patient's condition rapidly deteriorated with the development of cholinergic syndrome, so atropine was administered according to the symptoms. Despite the intravenous atropine the patient developed respiratory failure and hypotensive shock. Five hours post-admission he was intubated and mechanically ventilated. At reception serum cholinesterase activity was 341 ij/L (reference value is 4620–11,500 ij/L). Oximes were not available in the hospital, so he was treated with large doses of atropine by infusion. He needed dopamine stimulation for one day. The patient was on mechanical ventilation for 13 days, and received a total dose of 3082 mg of atropine. Because of the insecticide application in the cubital area there was a small necrosis. This wound was surgically treated after reception. Bullous changes were removed and it was covered with Vaseline gauze. With further treatment of this wound it improved greatly. **Conclusion:** Severe dimethoate poisoning was successfully treated with high doses of atropine. As atropine is ineffective at the nicotine receptors, and there was no possibility for oxime treatment, the patient needed prolonged mechanical ventilation. Mortality in dimethoate-poisoned patients may be greater than in those ingesting other pesticides due to hypotensive shock. In our case, the patient responded well to the treatment with dopamine and high doses of atropine. **References:** 1. Vučinić S, Joković D, Todorović V, et al. The experience of national poison control centre in management of acute organophosphorus insecticide (OPI) poisoning. Proceedings from CBMTS-IV. Spiez, Switzerland; 2002:51–4. 2. Singh S. Organophosphorous poisoning: an evidence based approach. MJAFI 2004; 60:2–4.

### 319. Chlorpyrifos

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**Objective:** Suicide attempts following exposure to organophosphate insecticides are not frequently seen in the United States. We present a case of organophosphate exposure complicated by intermediate syndrome. **Case report:** A 66 year old bipolar female was brought to our emergency department one hour after drinking an estimated 24 oz of a 6% chlorpyrifos solution in an attempted suicide. Rhinorrhea, increased salivation, and diarrhea were noted. Initial vital signs demonstrated a temperature of 36.8°C, heart rate of 97 beats per minute, respiratory rate of 18 breaths per minute, blood pressure 120/78 mm Hg, and an oxygen

saturation of 99% on 100% FIO<sub>2</sub> by non-rebreather mask. Coarse breath sounds and miosis were noted. Atropine and pralidoxime administration improved her symptoms. She received a total of 7 mg of atropine, 600 mg of pralidoxime, and 50 mg of diphenhydramine before being placed on a pralidoxime drip at 8 mg/kg/hour. Phenobarbital 130 mg IV every 8 hours was started to aid end-product metabolism. She was admitted to the ICU and developed respiratory failure requiring intubation. Pralidoxime and phenobarbital were continued. An atropine drip was started and titrated to effect. The patient was extubated on hospital day (HD) 9. Pseudocholinesterase levels became undetectable, while red blood cell (RBC) acetylcholinesterase remained essentially unchanged. She developed progressive ascending muscle weakness with loss of her gag reflex, and was reintubated on HD 11. She failed subsequent attempts at extubation and a tracheostomy was performed on HD 19. She was able to move her eyes, shake her head to questioning, and wiggle her hands and feet at the time of transfer to an extended care facility. **Conclusion:** We presented a case of chlorpyrifos toxicity following a suicide attempt. The patient developed the cholinergic signs characteristic of this exposure. RBC acetylcholinesterase levels remained unchanged, suggesting adequate initial pralidoxime dosing. However, the patient developed progressive weakness following apparent recovery. This may have represented chlorpyrifos redistribution from adipose stores. Intermediate syndrome may have also accounted for this change. While not frequently seen in the United States, this case helps remind practitioners of the toxicity of organophosphate insecticides and their potential use as suicidal agents.

### 320. Chronic Encephalopathy after Acute Poisoning with the Sarin Analogue Diisopropyl Fluorophosphate

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**Objective:** Chronic neurological disabilities occur in humans after acute poisoning with sarin. With a goal of developing acute antidotes to prevent the development of neurological disabilities, a rat model was developed of acute poisoning with the sarin analogue diisopropyl fluorophosphate (DFP). DFP was substituted for sarin because it has similar toxicity, is less volatile, poses a lower risk to investigators, and is readily available. **Methods:** Institutional Animal Care and Use Committee (IACUC) was obtained. Long Evans rats weighing 250–275 grams were randomized to: DFP group (N = 4): Rats received a single intraperitoneal (IP) injection of DFP (5 mg/kg). Control group (N = 4): Rats received a single equal volume IP injection of isopropyl alcohol, the vehicle in which the DFP was dissolved. After injection, rats were monitored for signs and symptoms of cholinesterase toxicity. If toxicity developed, antidotal therapy was initiated with atropine (2 mg/kg) and pralidoxime (25 mg/kg) and repeated as needed. Prior to injections and for four weeks thereafter, rats underwent neurological testing that included: Beam Walk for assessment of motor coordination and balance, Grip Strength for assessment of forelimb strength, Plus Maze for assessment of anxiety, Morris Water Maze for assessment of spatial learning and reference memory. **Results:** All rats in the DFP group developed significant toxicity requiring antidotal

rescue, while no rats in the control group developed symptoms after the injection. Within 2 weeks of exposure, rats poisoned with DFP took significantly longer to find the platform with repeated trials using the Morris Water Maze than control rats ( $19.0 \pm 3.1$  versus  $8.0 \pm .91$  at 13 days). These results were statistically significant with  $P < 0.05$  at days 13, 24 and 29. Other tests did not achieve statistical significance during the 4 week period. **Conclusion:** This rat model of DFP poisoning with antidotal rescue is a promising candidate for further studies to develop treatments to prevent delayed encephalopathy after poisoning. This pilot experiment suggests that the observation period be longer than 4 weeks. A power analysis suggested that 10 animals be included in each group in future studies. Since acute treatment with atropine and pralidoxime did not prevent the development of memory deficits, other acute therapies need to be found.

### 321. When Collaboration Between an Intensivist, Clinical Toxicologist and Analytical Toxicologist Leads to the Diagnosis of Severe Intoxication with Aldicarb.....

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**Objective:** Diagnosis of poisoning by aldicarb following an initial unexplained coma. **Case report:** Mrs L, 43 years old was admitted by the emergency medical service because of an unexplained muscarinic syndrome (vomiting, profuse diarrhea, bronchorrhea, miosis, coma (Glasgow scale 6)) with respiratory distress related to an inhalation, requiring mechanical ventilation. The administration of 1 mg of atropine intravenously gave brief improvement. The patient's history included starting a low-calorie diet. In the intensive care unit, the examination (CT scan without injection, lumbar puncture, ECG) was normal. Biological findings included hypokalemia, and signs associated with the respiratory distress. The patient recovered, and was discharged from hospital on day 11 without etiological diagnosis detected. The same evening, the patient developed a new muscarinic toxidrome with coma, severe respiratory distress requiring mechanical ventilation and was admitted to the intensive care unit. The poison center was contacted and recommended the administration of pralidoxime sulfate and assays; the assays in serum H + 8 showed: serum cholinesterase  $< 1000$  IU/L ( $N > 3000$  IU/L), aldicarb 5700 micrograms/L, aldicarb sulfone 58 micrograms/L, aldicarb sulfoxide 4500 micrograms/L. The assays in urine H + 30 showed: aldicarb 12 micrograms/L, aldicarb sulfone 467 micrograms/L, aldicarb sulfoxide 18000 micrograms/L. Literature describes serum aldicarb level of 850 to 900 ng/mL for severe poisoning, urine level from 250 to 1000 ng/mL. Mrs L recovered without sequelae and other complaints. **Conclusion:** Aldicarb which is prohibited in the EU since April 30, 2007 is a reversible inhibitor of cholinesterase. However, stocks are still available and so it remains a chemical which toxicologists must take into account in case of unexplained muscarinic syndrome. This diagnosis was made possible by the collaboration between the intensivist and toxicologists, as described in a previous case.<sup>1</sup> **Reference:** 1. Braganca C, Labadie M, Crenn A, et al. Criminal poisoning with aldicarb. Clin Toxicol 2011; 49:256.

### 322. Acute Strychnine Poisoning: A Case Report

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**Objective:** Strychnine is still used in veterinary medicine and as a rodenticide. Although rare, strychnine poisonings are potentially fatal and can easily be misdiagnosed, especially in cases with lack of information. This poison is a well-known competitive antagonist of the inhibitory neurotransmitter glycine at receptors in the spinal cord, brain stem and higher centers. Its action results in increased neuronal activity and excitability, leading to increased muscular activity. **Case report:** A 47-year-old man was found with convulsions on the street and was taken to the Emergency Medicine Hospital, Sofia after receiving 10 mg diazepam IM. Upon admission he was agitated, with marked tremor of upper extremities and had a series of tonic-clonic seizures in the admission room. During the diagnostic process it was discovered that approximately 2 hours earlier he drank a solution, containing "about 80 mg white powder" dissolved in water (this was later confirmed to be strychnine). Immediate treatment with high doses of diazepam, phenobarbital and pyridoxine was started; gastric lavage with activated charcoal was performed after controlling the initial convulsions; oxygen via nasal tube and IV fluids were given. He had elevated blood pressure up to 180/105 mmHg and mild tachycardia (up to 102–110 beats/minute). Strychnine was identified by using high performance thin layer chromatography (HPTLC) and confirmed by GC-MS in the same urine sample. Blood strychnine level could not be measured at the time of hospitalization. The patient continued to be conscious with marked muscle spasms of various muscles – neck, chest, and legs; followed by pain in the respective muscle groups for the next 4 days despite treatment. No respiratory arrest was observed. Laboratory data revealed mild acidosis on day 1–2; mild rhabdomyolysis without renal impairment was registered on day 3–4. **Conclusion:** We describe a case of strychnine poisoning with favorable outcome (first case in the last 20 years). Patient presented early, symptoms were recognized promptly and adequate and rapid supportive treatment started immediately. Strychnine ingestion should be considered as potentially fatal and the patients should be admitted for close observation and appropriate treatment since severe, life-threatening complications have been reported after ingestion of even small amounts. Patients should be carefully monitored as they can deteriorate rapidly.

### 323. Life-Threatening Severe Metabolic Acidosis Treated with Renal Replacement Therapy Following Triclopyr Ingestion

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**Objective:** Triclopyr is a pyridine-based selective herbicide. It is classified as moderately hazardous. Severe intoxication following triclopyr ingestion has generally not been found, except in one case report.<sup>1</sup> We present a case of severe metabolic acidosis treated with renal replacement therapy following triclopyr ingestion. **Case report:** A 63-year-old man presented to a local hospital with a comatose mental state following ingestion

of about 200 mL of a triclopyr herbicide (30% triclopyr triethylamine salt, 4.5% polyoxyethylene nonylphenol surfactant, and 65.5% water). The patient underwent tracheal intubation and gastric lavage, and was then referred to our emergency department for further management. On admission, blood pressure was 60/40 mmHg, pulse 116, and SaO<sub>2</sub> 96%. The patient was ventilated manually and arterial blood gas analysis showed pH 7.006; PaCO<sub>2</sub> 6.4 kPa; PO<sub>2</sub> 20.7 kPa; and HCO<sub>3</sub> 11.4 mmol at an inspired oxygen level of 10 L/min. The serum lactate was 18.0 mmol/L. The electrocardiogram showed sinus tachycardia, but was otherwise normal. Echocardiogram showed a hyperdynamic wall motion without regional wall motion abnormalities. Norepinephrine, dopamine, crystalloid, and bicarbonate were administered for hypotension and severe acidosis. In spite of sustained shock, the patient showed well-maintained urine output with maximally 750 mL/h, and generally looked hyperemic. The continuous renal replacement therapy was started at 7 hours after ingestion, since the metabolic acidosis was not relieved despite fluid resuscitation. Metabolic acidosis was completely relieved at 12 hours after the use of renal replacement therapy. Vasopressor infusion was discontinued and the patient regained alertness on hospital day 2. The patient was extubated at 48 hours after ingestion and discharged from the intensive care unit on hospital day 3. **Conclusion:** Triclopyr usually causes insignificant effects. However, triclopyr poisoning can lead to life-threatening metabolic acidosis and shock. The toxic mechanism of triclopyr in humans is presumed to be the systemic vasodilation and inhibition of oxygen utilization rather than cardiotoxicity, in terms of high urine output, generalized hyperemia, and lactic acidosis. Renal replacement therapy should be considered in severe acidosis following triclopyr ingestion. **Reference:** 1. Kyong YY, Lee KU, Choi KH. Severe systemic intoxication following triclopyr-TEA ingestion. Clin Toxicol (Phila) 2010; 48:942–4.

### 324. Poisonings from Ingestion of Chlorate-Containing Herbicides

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**Objective:** Chlorates are strong oxidizers and used as ingredients in matches, explosives and dyestuffs as well as herbicides. Although commercial use of chlorate-containing weed killers is banned within the EU, they can still be purchased by private consumers as "stone cleaners" in large quantities, i.e. in containers with up to 10 kilograms. We report on three cases of chlorate poisoning that occurred in spring 2011. **Case series:** Accidental ingestion of a sip from a glass containing a (table?)spoonful of sodium chlorate dissolved in water was asymptomatic in a male adult after gastric lavage, activated charcoal and laxative within 2 hours after ingestion. Inappropriate storage of a chlorate solution in a beverage bottle led to accidental ingestion of a sip by a 59-year-old man and resulted in gastrointestinal symptoms and haemolysis with acute renal failure. The patient recovered after haemodialysis. A 37-year-old man died in the course of multiple organ failure two days after suicidal ingestion of a larger quantity of potassium chlorate despite the administration of thiosulfate, methylene blue, toluidine blue, exchange transfusion and haemodialysis. **Conclusion:** A dose of 7.5 grams of potassium chlorate<sup>1</sup> and 15 to 35 grams of sodium chlorate<sup>2</sup>, respectively, has been lethal in adults. As strong oxidizers, chlorates can directly oxidize haemoglobin and even small doses may cause significant methaemo-

globinaemia and haemolysis which consequently lead to acute renal failure. In addition, chlorates may also be directly toxic to the proximal renal tubule. Treatment of methaemoglobinaemia with methylene blue and tonium chloride (toluidine blue), respectively, may have limited efficacy due to chlorate-induced inactivation of glucose-6-phosphate dehydrogenase, an enzyme required for reduction of methaemoglobin. Thiosulfate has been suggested to inactivate the chlorate ion by reduction to the chloride ion, however, the efficacy of thiosulfate administration has not been confirmed. Exchange transfusion and haemodialysis may be efficient in patients with severe poisoning.<sup>3</sup> *References:* 1. Bernstein R. Kaliumchlorat-Vergiftung. Arch Exp Path Pharmacol 1930; 1:15–6. 2. Helliwell M, Nunn J. Mortality in sodium chlorate poisoning. Br Med J 1979; 1:1119. 3. Nelson LS, Lewin N, Howland MA, et al, eds. Goldfrank's Toxicologic Emergencies. 9th ed. New York, USA: McGraw-Hill, 2010.

### 325. A Case of Delayed Neuropathy Following an Intentional Carbamate Ingestion

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*Objective:* Carbaryl is a widely used and easily accessible carbamate (CB) insecticide that causes reversible inhibition of acetylcholinesterase (AChE). Organophosphate (OP) induced delayed peripheral neuropathy (OPIDN) resulting in paralysis has been described in the literature; however, this phenomenon is rarely reported following CB exposures given the spontaneous hydrolyzation of the CB-AChE bond and relatively short duration of symptoms. We report a case of delayed neuropathy following an intentional CB ingestion. *Case report:* A 24-year-old man was admitted to the intensive care unit (ICU) after the intentional, witnessed ingestion of carbaryl (Sevin®) in a suicide attempt. His initial vital signs were notable for hypertension (BP 166/109 mmHg), tachycardia (pulse 113), and tachypnea (respiratory rate 22). He was afebrile with oxygen saturations of 98% on room air, and his neurologic examination was non-focal. His lactate was elevated at 4.0 mEq/L, serum bicarbonate measured 26 mEq/L, and creatinine was 1.2 mg/dL. Ethanol, ethylene glycol, salicylate, and acetaminophen concentrations were negative. His respiratory status worsened, and 4 days after admission, his chest X-ray showed pneumomediastinum. He was transferred to a tertiary hospital and had 5 chest tubes and 2 Blake drains (pericardial, subcutaneous) placed in the operating room. Three days post-operatively, the patient was unable to move his extremities. Magnetic resonance imaging (MRI) of the brain and spinal cord was normal, and his electromyography (EMG) revealed a peripheral sensory motor neuropathy. *Conclusion:* Peripheral neuropathies have been described following acute exposures to OPs. Although rare, there are 3 case reports of delayed neuropathy (sensory and motor) following exposure to CBs in the literature. This case provides additional evidence for the development of this phenomenon. In this case, spinal cord ischemia and other central etiologies were excluded by MRI, and there were no other readily identifiable toxicologic exposures to account for his symptoms. This case highlights the potentially devastating development of a mixed motor and sensory peripheral neuropathy following carbamate exposure. Healthcare providers should be aware of this complication when treating patients who have ingested CBs.

### 326. Clinical and Radiology Findings in Hydrocarbon Poisoning in Children: A Five Year Period Study

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*Objective:* To study the clinical and radiology manifestations in hydrocarbon poisoning in children. *Methods:* We performed a retrospective study regarding hydrocarbon poisonings admitted to a pediatric toxicology department during a five year period. We used medical records, taking into consideration the following criteria: type of hydrocarbon, route of poisoning, type of clinical manifestations and radiology findings. *Results:* 87 children with hydrocarbon poisoning were admitted to our department between 2007–2011. In all cases the poisoning was produced by ingestion. The following hydrocarbons were involved: solvent for varnishes and paint 56 cases (64.3%), petrol 9 cases (10.3%), acetone 8 cases (9.1%), lamp oil 8 cases (9.1%), diesel oil 6 cases (6.8%). The following clinical manifestations were recorded: gastrointestinal symptoms in 43 patients (solvent for varnishes and paint 29, out of which one case haematemesis; acetone 4 cases; petrol 4 cases; lamp oil 3 cases; diesel oil 2 cases); neurological symptoms (headache, dizziness, consciousness disorders) in 8 cases (solvent 6 cases out of which 2 with coma, and diesel oil 2 children); respiratory manifestations in 11 cases (acute pneumonia presenting on X-ray film unilateral or bilateral opacities 6 cases, out of which 2 with diesel oil poisoning and 4 cases with solvent poisoning; bilateral pneumonia with pneumothorax and pneumomediastinum in one case with diesel oil poisoning; cough in 4 cases (diesel oil and solvents). Twenty-one patients were asymptomatic (10 cases with solvent, 5 cases acetone, 3 cases lamp oil, 2 cases petrol, one case diesel oil). *Conclusion:* In the majority of cases with hydrocarbon poisoning in children mild symptoms were recorded (gastrointestinal, cough, cephalgia, dizziness) or no symptoms. Diesel oil and solvent produced poisonings with the most severe manifestations such as coma or severe pneumonia. *References:* 1. Lewander W, Aleguas A. Petroleum distillates and plant hydrocarbons. In: Shannon MW, Borron SW, Burns M, eds. Haddad and Winchester's Clinical Management of Poisoning and drug overdose. 4th ed. Philadelphia, USA: Saunders Elsevier, 2007:1343–6. 2. Hoffman RS. Respiratory Principles. In: Flomenbaum N, Goldfrank L, Hoffman R, et al, eds. Goldfrank's Toxicologic Emergencies. 8th ed. New York, USA: McGraw Hill, 2006:352–8.

### 327. Pulmonary Injury in Acute Poisoning in Children: A Five Year Study

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*Objective:* To evaluate the incidence, etiology, type and severity of pulmonary injury in acute poisoning in children. *Methods:* We performed a retrospective study of acute poisoning with pulmonary injury, admitted to our department during a 5 year period, using medical reports and taking into consideration the following criteria: type of substance, type of pulmonary injury, clinical and radiological manifestation, outcome. *Results:* Out of

the 2604 poisoned children admitted to our department between 2007–2011, 47 (1.76%) presented pulmonary injury. The following types of injury were noted: acute lung injury (non cardiogenic oedema and diffuse bilateral infiltrates): 27 cases, unilateral or bilateral acute pneumonia in 15 cases, pleural effusion in 4 children, pneumothorax and pneumomediastinum in 1 case. Noncardiogenic oedema manifested with: dyspnea, bubbling rales, tracheobronchial hypersecretion and diffuse bilateral infiltrates on pulmonary radiography, was present in 27 cases (19 children with acute severe poisoning with acetylcholinesterase inhibitors and 8 with severe carbon monoxide poisoning). Acute pneumonia (15 cases) manifested with fever, cough, dyspnoea, rales unilateral radio-opacity or bilateral small opacities had the following etiology: petroleum distillates 13 cases, charcoal aspiration 2 cases. Pleural effusion was noted in 4 cases; 2 children with petroleum distillate poisoning and 2 with caustics – sodium hydroxide poisoning. *Conclusion:* Pulmonary injury is a rare complication in acute poisoning in children having, however, high severity potential. Acute noncardiogenic pulmonary oedema is the most frequent type of pulmonary injury noted in acute poisoning in our statistics while charcoal aspiration pneumonia is a very rare entity. *References:* 1. Holland MG. Pulmonary Toxicology. In: Shannon MW, Borron SW, Burns M, eds. Haddad and Winchester's Clinical Management of Poisoning and drug overdose. 4th ed. Philadelphia, USA: Saunders Elsevier, 2007:167–88. 2. Hoffman RS. Respiratory Principles. In: Flomenbaum N, Goldfrank L, Hoffman R, et al, eds. Goldfrank's Toxicologic Emergencies. 8th ed. New York, USA: McGraw Hill, 2006:352–358.

### 328. Acetylene Induced Interstitial Pneumonitis

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*Objective:* Acetylene is a colorless gas commonly used for welding. It mainly acts as a simple asphyxiant, but we present here a patient who developed severe interstitial pneumonitis after acetylene exposure during aluminum welding. *Case report:* A 44-year old man with no previous medical history was welding with acetylene, argon and aluminum electrode sticks in a non-ventilated aluminum tank for 2 hours. Immediately after welding he felt dizzy and weak. The dizziness disappeared in the first hour while breathing fresh air, but 4 hours after welding he became worse with progressive shortness of breath. Twenty-two hours after welding he arrived at the Emergency Department due to severe dyspnea and respiratory insufficiency with pO<sub>2</sub> 6.7 kPa. The chest X-ray showed diffuse interstitial infiltration. Pulmonary function and gas diffusion tests revealed severe restriction (55% of predictive volume) and impaired diffusion capacity (47%). Toxic interstitial pneumonitis was diagnosed and high-dose systemic corticosteroid methylprednisolone (1 mg/kg/day) and inhalatory corticosteroid fluticasone (0.5 mg/12 hours) therapy was begun. Computed tomography (CT) of the lungs showed a diffuse patchy ground-glass opacity with no signs of small airway disease associated with interstitial pneumonitis. The patient's symptoms, arterial oxygenation, pulmonary function and gas diffusion tests rapidly improved during the first week. The chest X-ray completely normalized. The patient was discharged on the ninth day, but corticosteroid therapy was continued for 8 weeks with gradually reduced doses. The patient's follow-up during 8 weeks of corticosteroid therapy and for 5 months afterwards revealed a second transient

deterioration in respiratory function between 2 and 7 weeks after welding that completely normalized 5 months later. CT of the lungs 5 months after welding was completely normal. **Conclusion:** Interesting in this patient was delayed interstitial pneumonitis with severe respiratory distress several hours after welding that was most probably the result of acetylene exposure, since the patient had no signs of metal toxicity, particularly metal fume fever. Toxic interstitial pneumonitis after acetylene exposure improves after early systemic and inhalatory corticosteroid therapy, but a high dose of corticosteroids should probably be prolonged beyond one week due to transient deterioration of respiratory function after the first week.

### 329. Unexplained Death Associated with a Rust Remover Spray

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**Objective:** A 69-year-old male had treated the underbody of his car with a lubricant/penetrating oil. He had used a commercial rust remover spray consisting of petrol hydrocarbons, carbon dioxide as a propellant and molybdenum disulfide. The spray had been applied in a lying position under the car for about 15 minutes. The patient developed acute nausea, dyspnoea and circulatory shock. **Case report:** When the emergency medical service arrived after a few minutes, they found the patient already in a pulseless and cyanotic condition. Immediate resuscitation measures resulted in a stabilization of circulation in the still unconscious patient on the scene after about 40 minutes, and he was admitted to the intensive care unit of a hospital. On admission, the deeply comatose patient, showed the typical signs of a circulatory shock and died four hours later. In post-mortem findings no recent myocardial damage was found and macroscopic examination of the lungs did not result in any pathological findings that could have explained the patient's death. The patient died in the intensive care unit of a hospital *circa* four hours after the onset of first symptoms after spraying with a rust remover in a lying position under the car. No serious diseases were reported in the deceased patient's medical history. An obvious cause of death was not stated in the post-mortem records. According to the present state of knowledge gained from comparable accident reports, especially from investigations of the German "Magic Nano Case Series" more and more indications have suggested that the possibly toxic effect on the lungs may be attributed to additives or solvents contained in aerosols. It may also be assumed that the very fine dispersion of the spray mist results in critical droplet sizes so that components of the chemical product may penetrate deeply into the smallest alveoli and cause serious toxic effects in these structures. **Conclusion:** The unexplained death associated with a rust remover spray could be attributed to additives or solvents contained in aerosols. This should be the source of further research.

### 330. Respiratory Disorders after Use of Waterproofing Sprays – Scientific Findings for 'Magic Nano' Sealing Sprays Giving Plausible Explanations for the 'Waterproofing Spray Syndrome'

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**Objective:** In March 2006, cases of in part severe pulmonary health impairment were observed after normal

use of 'Magic Nano' sealing sprays in Germany. In contrast, a previously marketed 'Magic Nano' pump spray (without propellants) had not caused any problems. Based on a rapid and complete documentation of more than 150 cases in collaboration with the German Poison Control Centers, the BfR immediately initiated a recall. The public as well as authorities and ministries were informed by timely publication of press releases based on nine BfR and EU expert meetings. **Methods:** Supported by the BfR Committee 'Assessment of Poisonings' we started different scientific investigations: 1) Literature research 2) Physico-chemical examinations of 'Magic Nano' and comparable waterproofing spray aerosols 3) Animal tests (OECD protocol 403) and 4) Cells tests for *in vitro* studies of aerosols. **Results:** Investigations into the composition of the product were considerably complicated, but already in May 2006, results were available showing that the products concerned did not contain any nano-sized inert particles. The hazardous manifestations associated with nano sealing sprays were very similar to the health problems documented in a number of earlier case clusters associated with leather and impregnating sprays. The studies in rats could explain the high occurrence of severe acute lung damage in humans. The results of the physico-chemical analysis showed that the severe lung damage due to 'Magic Nano' sprays was caused by a major share (> 10%) of ultrafine mass particles (UFP), which could be considered as carriers to the deep alveolar parts of the lungs. X-ray analysis showed typical elements (C, Si, Na, P, Cl, F) of the fluorosilanes. So a high part of UFP could plausibly explain a carrier transport of the toxic and water-protective semi-volatile fluorosilanes deeply into the alveolar areas, causing interference with the alveolar lung surfactant. **Conclusion:** Currently, in a following research project, the BfR is analyzing different spray formulations to find similarities to the "waterproofing sprays syndrome". In an isolated perfused rat lung model parallel to the chemical analysis of the aerosols, we have been able to find further evidence for the 'carrier thesis' for the 'waterproofing spray syndrome'.

### 331. Evaluation of Lung Toxicity by the Use of In Vitro Models

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**Objective:** Exposure to lung toxicants can lead to severe acute and chronic health effects. Detailed knowledge about the pathophysiology of chemicals is required for risk assessment and adequate therapy. Due to a wide variety of clinical toxicological pictures appropriate models are necessary. As ethical reasons demand the replacement of animal experiments, *in vitro* models that reflect the situation in human beings may fill the gap. **Methods:** Beside monocultures of lung epithelial cell and lung endothelial cells to examine *in vitro* lung toxicity, complex *in vitro* co-culture models of the proximal (bronchial model) and distal (alveolar model) respiratory system were established.<sup>1,2</sup> Mimicking the *in vivo* situation exposure was performed by using a Radial Flow System which allows air-liquid interface exposure. Depending on the model used for the experiments various parameters such as cell vitality, transepithelial electrical resistance (TER), inflammatory response (IL-6, IL-8), mucus production, apoptosis and necrosis were examined. Sulfur mustard (SM) and cadmium chloride were used for evaluation. **Results:** SM induced apoptosis

in A549 monocultures and in the alveolar model, which was accompanied by TER collapse, release of proinflammatory cytokines and histological changes. In the bronchial model SM showed comparable effects with additional increase of mucus production. Exposure of the alveolar model to cadmium showed side-specific biological effects where upon TER was mainly affected when the model was exposed on the basal side. **Conclusion:** It may be concluded that the *in vitro* models may be used as a valuable tool for evaluating the lung toxicity of harmful chemicals and for understanding the pathophysiology of lung toxicants. The *in vitro* models should also allow a widespread screening of potential drugs and antidotes. **References:** 1. Emmler J, Hermanns MI, Steinritz D, et al. Assessment of alterations in barrier functionality and induction of proinflammatory and cytotoxic effects after sulfur mustard exposure of an *in vitro* coculture model of the human alveolo-capillary barrier. *Inhal Toxicol* 2007; 19:657–65. 2. Papritz M, Pohl C, Wübbke C, et al. Side-specific effects by cadmium exposure: apical and basolateral treatment in a coculture model of the blood-air barrier. *Toxicol Appl Pharmacol* 2010; 245:361–9.

### 332. Chemical Decontamination: An Activity that should be Performed in Hospital Emergency Departments

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**Objective:** Exposure to chemical products producing cutaneous or ocular involvement is a cause of emergency department visits. The aim of this study was to describe the characteristics of patients treated by a tertiary hospital emergency department for chemical decontamination. **Methods:** We adapted a part of the emergency department for cutaneous and ocular decontamination of patients exposed to chemicals. We describe the chemical decontamination carried out over an 18-month period and evaluate patients' epidemiological characteristics, the toxic substance involved, the type of incident (home or work), clinical manifestations, treatment given and the evolution of cases. **Results:** We included 36 patients with a mean age of 42.8 (SD 16.7) years, of which 24 (66.7%) were female. The products most often involved were caustic substances (52.8%), solvents or degreasing agents (19.4%), adhesives (13.9%) and personal defence sprays (8.3%). Domestic (41.7%) and occupational (36.1%) accidents were the most-frequent causes, but there were also assaults (8.3%) and one suicide attempt. Involvement was ocular (75%), cutaneous (19.4%) or mixed (2 cases). The most-frequent ocular signs and symptoms were pain, itching, burning, stinging, blepharospasm, blurred vision, redness, and, in the case of adhesives, adhesion of eyelids. In skin exposures, patients had signs of irritation or first or second degree burns. One patient suffered facial involvement after ingesting sulphuric acid in a suicide attempt and died a few hours later. The initial treatment applied was water, soap and water or Diphoterine. All patients with ocular involvement were followed up: three presented mild sequelae. One patient with skin exposure reported sequelae. **Conclusion:** Exposure to chemicals is frequent, mainly as a result of domestic or occupational accidents, but also due to assaults and suicide attempts. There is a risk of sequelae and death.

### 333. Severe Lung Injury after Intravenous Injection of Firefighter Liquid in an Attempted Suicide

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**Objective:** Acute lung injury after aspiration of liquid hydrocarbons is well known while intravenous application is rare.<sup>1</sup> Few case reports illustrate severe haemorrhagic pneumonitis, multiorgan system failure (MOS) or death following the injection of small amounts of gasoline. We report on the clinical course of a patient following intentional intravenous infusion of 400 mL of firefighter liquid. **Case report:** A 21-year old man attempted suicide by intravenous infusion of 400 mL liquid hydrocarbon mixture via a 20 G cannula. He developed respiratory insufficiency requiring intubation and artificial ventilation. MOS with vasodilatory shock was treated with high doses of norepinephrine. Despite lack of proven therapeutic interventions, the patient underwent haemodialysis for 3 hours and subsequently received plasmapheresis with three litres of human albumin 5%. Chest computer tomography (CT) showed diffuse pulmonary infiltrates with bilateral pleural effusions that were drained. Empiric antibiotic therapy was instituted. Global cerebral oedema visible on cranial CT was treated with intravenous mannitol. Initial laboratory findings were normal. During the course of therapy thrombocytopenia (34,000/mcL, ref. 150,000–300,000/mcL), a decrease in serum cholinesterase (2275 U/L, ref. 5,100–11,700 U/L) as well as an increase of his CRP (385 mg/L, ref. < 5 mg/L), CK (977 U/L, ref. < 190 U/L) and INR (2.37, ref. 0.85–1.15) developed. Routine occupational blood investigation on hydrocarbons could not identify any hydrocarbon in blood samples. However, when using solid phase micro-extraction (SPME) and headspace GC/MS, branched C-12 alkanes and alkenes were detected in blood as well as in the tapped pleural fluid. Blood samples collected following haemodialysis and plasmapheresis demonstrated a substantial decrease in the hydrocarbon concentrations. **Conclusion:** Intensive care guided by the attempt to reduce the toxic load and treat severe symptoms led to a successful outcome following the intravenous injection of large doses of long chain aliphatic hydrocarbons. After haemodialysis and plasmapheresis the concentration of C12 alkanes and alkenes had substantially decreased. A causal relationship between the positive effects of these treatments and the observed change of hydrocarbon concentrations in the blood cannot necessarily be implied. **Reference:** 1. Layton TR, Grant KJ, Vilella ER. Gasoline injection. *J Toxicol Clin Toxicol* 1983–1984; 21:409–12.

### 334. Chronic Elemental Mercury Poisoning by Inhalation Accompanied by Positivity of a New Biomarker in Humans

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**Objective:** Chronic poisoning may result after prolonged mercury (Hg) vapor inhalation from broken devices (i.e. thermometers, barometers). We report a case of chronic poisoning from long exposure to Hg vapor from a large broken barometer at home. **Case report:** A 72 year-old man (70 kg body-weight) presented to our Toxicology Unit with a 10 year medical history of progressive neurological symptoms. The patient's occupational history was negative for previous exposure to metals. The patient referred to a broken barometer maintained near a heating source in his home study-room during the last ten years. First toxicological evaluation confirmed the neurological picture previously reported, characterized by motor ataxia, increased motor tone, sensory deficits in touch at inferior limbs. Neurophysiological tests revealed mild axonal sensory-motor polyneuropathy at superior/inferior limbs. A nuclear magnetic resonance performed 5 years before was negative. Blood (BHg) and urine (UHg) Hg levels at admission were 27 and 1.4 micrograms/L respectively (normal value BHg 1–4.5 and UHg 0.1–4.5 micrograms/L). BHg and UHg after DMSA mobilization-test were 24.5 and 5.2 micrograms/L. Elemental-Hg and methyl-Hg were evidenced at BHg speciation. Two biomarkers of Hg neurotoxicity were achieved, showing a normal platelet monoamine-oxidase-B activity of 10.46 nanomol/mg prot/hr (normal value 7.0–11.0) and a strong elevation in lymphocyte-muscarinic-receptors of 205.43 femtomol/million lymphocytes (normal value 8.0–16.0). Two cycles of chelating therapy with oral DMSA (2400 mg/day for 5 days followed by 1600 mg/day for 14 days) were administered and a gradual improvement in clinical manifestations with a progressive reduction of BHg and UHg were obtained. **Conclusion:** Gradual volatilization of elemental Hg may result in chronic toxicity both in occupational and home settings. Lymphocyte-muscarinic-receptors elevation has been shown to be sensitive/predictive targets for methyl-Hg neurotoxicity in animal studies.<sup>1</sup> In our case, history, clinical manifestations and Hg levels confirmed the diagnosis; the strong elevation in lymphocytes-muscarinic-receptors seems to be in this first documented case a sensitive biomarker in chronic elemental Hg poisoning in humans. **Reference:** 1. Coccini T, Randine G, Candura SM, et al. Low-level exposure to methylmercury modifies muscarinic cholinergic receptor binding characteristics in rat brain and lymphocytes: physiologic implications and new opportunities in biologic monitoring. *Environ Health Perspect* 2000; 108:29–33.

### 335. Absorption of Elemental Mercury by Inhalation from Broken Clinical Thermometers in Heating Sources: Evaluation of a Case Series

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**Objective:** Elemental mercury (Hg) is absorbed primarily via inhalation of vapors. Hg is moderately volatile at room temperature but significantly evaporates when heated or aerosolized. A case series with blood/urine mercury levels after accidental Hg inhalation from broken mercury-in-glass medical thermometers in heating sources is described. **Case series:** A retrospective analysis (2004–2011) produced 16 cases (age 0.5–75 years) referred to the Pavia Poison Centre (PPC). All

patients inhaled Hg vapors from broken thermometers in heating sources such as boiling water (n = 6), boiling soup (n = 6), heated homogenized baby food (n = 2), gas stove (n = 1) and boiled stew (n = 1). The average time of exposure was 35 minutes (10–60 minutes). All patients were asymptomatic. Urine and blood or plasma samples were collected and analyzed after an average time of 6 hours (range 1–24 hours) from exposure. In 8/16 patients mercury levels were normal either in urine (normal value 0.1–4.5 micrograms/L) and in blood (normal value 1–4.5 micrograms/L) or plasma (normal value 0.1–1.5 micrograms/L). The remaining 8/16 patients had a minimal increase in mercury levels. Among these, 2 patients exposed to Hg in boiling water presented a minimal increase either in urine and blood levels (11.3, 5.4 and 9, 4.9 micrograms/L respectively). Mercury plasma levels were slightly elevated in 2 other patients (3 and 2.1 micrograms/L) exposed to Hg in boiling water and soup respectively. In the last 4 patients only urine levels were raised (range 6.1–6.5 micrograms/L) and 3 of these inhaled Hg in boiling water. **Conclusion:** Toxicity from elemental mercury most commonly arises in the occupational setting. Hg vapors may develop from broken thermometers in or near heating sources or from improper handling in the home setting.<sup>1</sup> In our case series mercury levels obtained during the first hours after short term exposure were normal in half the patients (8/16). Slight elevation in mercury levels mainly occurred from broken thermometers in boiling water but did not result in acute toxicity. **Reference:** 1. Baughman TA. Elemental mercury spills. *Environ Health Perspect* 2006; 114:147–52.

### 336. Knowledge of Intralipid® in Emergency Departments

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**Objective:** To assess awareness amongst Emergency Department (ED) doctors about the role of “lipid rescue therapy” (Intralipid®) in treating drug toxicity. **Methods:** We carried out a survey of doctors in Irish Emergency Departments to assess their knowledge of Intralipid®. Eight questions covered topics including indications, dose, local availability, and previous use of Intralipid®. The survey was conducted using telephone, face-to-face interviews, and Survey Monkey®. For comparison purposes, we also surveyed a random sample of anaesthetists. **Results:** 74 ED doctors completed the survey. Sixty-seven per cent of respondents were Registrar or Consultant grade. Only 2 ED doctors had previously used Intralipid® to treat drug toxicity; in both cases for lignocaine toxicity. When asked which drugs might respond to Intralipid® therapy, 45% of ED doctors did not know, 36% said local anaesthetics and 23% said lipid soluble drugs. Twenty per cent also said tricyclic antidepressants (TCAs) and/or verapamil. Unsurprisingly, 96% of anaesthetists (n = 122) said local anaesthetics. Thirty-two per cent also said lipid soluble drugs, and 22% said TCAs and/or verapamil. Sixty per cent of ED doctors were not aware of any guidelines to calculate the dose of Intralipid® while 27% would use TOXBASE® guidelines. Most anaesthetists (84%) said they would use guidelines issued by the Association of Anaesthetists in Great Britain & Ireland (AAGBI); only 14% of ED doctors said they would use these guidelines. When asked about local availability, 95% of anaesthetists knew Intralipid® was available in their hospital despite the fact that only 6% of this group had ever used it. Of note, 78%

of ED doctors did not know whether Intralipid® was available in their hospital. **Conclusion:** A growing number of recent publications have assessed the potential benefits of Intralipid® as a therapy in poisoning.<sup>1</sup> Conclusive indications for use have yet to be established, but anecdotal evidence suggests it may have a role in the treatment of drug toxicity. Despite this, our findings suggest that knowledge about Intralipid® is limited among doctors in Irish Emergency Departments; further education in this area is recommended. **Reference:** 1. Cave G, Harvey M, Graudins A. Intravenous lipid emulsion as antidote: A summary of published human experience. *Emerg Med Australas* 2011; 23:123–41.

### 337. Delayed Bowel Necrosis Following Overdose of Sustained-Release Verapamil

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**Objective:** To describe a case of delayed bowel necrosis requiring total colectomy following an intentional overdose of sustained-release verapamil. **Case report:** A 41 year old woman presented 2 hours after ingesting 30 Calan-SR 240 mg tablets. She received oral activated charcoal, IV calcium gluconate and IV fluids and was transferred to the ICU of a regional tertiary hospital where she arrived asymptomatic. Vital signs were normal until 14 hours after the ingestion. Bradycardia was her initial sign of toxicity (HR in 40s), followed by hypotension (60 mmHg systolic), then complete heart block and obtundation. Subsequent therapeutic interventions included IV calcium drip, atropine, endotracheal intubation, infusions of norepinephrine, epinephrine, dopamine, isoproterenol, vasopressin, and dopamine, hyperinsulin-euglycemia therapy (HIE), transvenous pacer placement, nitrous oxide, hydrocortisone, hemodialysis and 48 hours of continuous intravenous lipid emulsion therapy (ILET). By day 8, she had made a full hemodynamic recovery and was off all pressors, HIE, and transvenous pacing, though she was still intubated. She was expected to recover fully, but on day 9 developed black stools and fevers. The origin of the fever was initially unclear and the etiology of black stools was felt to represent passage of activated charcoal and considered a good sign of bowel motility. On day 14 she underwent abdominal computed tomography (CT) to work up the persistent fever. Colonic pneumatosis was discovered. She underwent emergent laparotomy at which time her entire colon was found to be necrotic and therefore resected. She ultimately recovered and was discharged to rehab 2 months after admission. **Conclusion:** We present a case of delayed toxicity and bowel necrosis requiring total colectomy following a verapamil overdose.

### 338. Acute Midodrine Overdose: A Case Series

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**Objective:** Midodrine is a prodrug of desglymidodrine (DGM), which activates alpha-1-adrenergic receptors of the arteriolar and venous vasculature<sup>1</sup>, and has been approved for the treatment of orthostatic hypotension. The recommended therapeutic

**Table 1.** Patients characteristics, midodrine dose, signs and symptoms with classification according to severity (Poisoning Severity Score).

Patient	Midodrine ingested dose		Pulse bpm	Blood pressure (mmHg)	Symptoms/signs	Severity
	mg	mg/kg				
0.1 y/o female	2	0.5	100	110/70	Absent	minor
1.5 y/o female	2.3	0.2	100	76/55	Absent	unclassifiable
1.7 y/o male	2.5	0.23	130	n.a.	Absent	unclassifiable
14 y/o male	50	0.71	mild bradycardia	mild hypertension	Anxiety, hyperventilation	minor
16 y/o female	125	2.08	47	183/108	Nausea, headache	moderate
23 y/o female	58	n.a.	52	169/100	Nausea, vomiting	minor
28 y/o female	50	n.a.	39	142/90	Absent	severe
32 y/o female	100	n.a.	35	180/100	Nausea, vomiting	severe
35 y/o female	130	n.a.	38	140/80	Lethargy	severe
60 y/o female	30	n.a.	43	164/90	Nausea, shivering	moderate

dose is 10 mg. Information on overdose with this antihypertensive agent is limited to reports from the producer, in which two adults developed hypertension, and one additionally bradycardia and CNS depression, following the ingestion of 205 and 250 mg, respectively.<sup>2</sup> **Methods:** Retrospective analysis of all acute midodrine monointoxications involving children and adults, reported by physicians to the Swiss Toxicological Information Centre (STIC) between January 1995–September 2011 with written feedback on clinical course. **Results:** Four children and 6 adults could be included. Three patients experienced severe bradycardia (35–39 bpm) after ingestion of 50–130 mg midodrine. An ECG was available in 3 bradycardic patients and showed sinus bradycardia. All patients recovered without sequelae. (Table 1) **Conclusion:** Midodrine poisoning after moderate overdoses can cause marked bradycardia without significant hemodynamic compromise. Mild bradycardia has been described as an adverse reaction to midodrine, and may be due to both vagal reflex mechanisms and a decrease of sympathetic nervous system activity due to the augmented venous return. Further symptoms were consistent with adverse effects which have been described in clinical trials. Complete recovery can be expected with supportive care. **References:** 1. Lamarre-Cliche M, Souich P, Champlain J, et al. Pharmacokinetic and pharmacodynamic effects of midodrine on blood pressure, the autonomic nervous system, and plasma natriuretic peptides: a prospective, randomized, single-blind, two-period, crossover, placebo-controlled study. *Clin Ther* 2008; 30:1629–38. 2. Product Information: ProAmatine®, midodrine. Roberts Pharmaceutical Corporation, Eatontown, NJ, 1998.

### 339. Risk of Bicarbonate Therapy in Overdose Patients with Prolonged QT

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**Objective:** Hypertonic sodium bicarbonate is indicated for overdose patients with widened QRS to prevent ventricular dysrhythmias due to sodium channel blockade. However, the efficacy and risk of bicarbonate for this indication remain unclear. This nonrandomized study evaluates the efficacy and risk of bicarbonate in acutely

overdosed emergency department (ED) patients. **Methods:** Consecutive adult (> 18 years) ED patients with acute overdose at one urban, tertiary care hospital were eligible over 14 months (2009–10). Subjects with a wide QRS (> 100 ms) were studied and the nonrandomized decision to initiate bicarbonate was made by the treating physicians. Baseline data included demographics, toxicology screens, and computer-interpreted intervals on the presentation ECG. Subjects were prospectively followed for the in-hospital occurrence of any adverse cardiovascular event (ACVE) defined as the occurrence of  $\geq 1$  of the following: myocardial injury (troponin > 0.09 ng/mL), shock (hypotension requiring vasopressors), ventricular dysrhythmia (VT, VF, or torsade de pointes (TdP)), and cardiac arrest (loss of pulses requiring cardiopulmonary resuscitation (CPR)). **Results:** Of 391 screened ED patients 89 (mean age 44.9, 64% male) with wide QRS were included for analysis (mean QRS 113  $\pm$  20 ms, mean QTc 437  $\pm$  37). Most frequent drugs were benzodiazepines (10), opioids (9 total, 5 methadone), tricyclic antidepressants (TCAs) (7), cocaine (5), and diphenhydramine/doxylamine (4). There were 13 (14.6%) ACVE including 3 ventricular dysrhythmias (3.4%), and 3 deaths (3.4% mortality). Bicarbonate was given in 10 patients (3 TCAs, 2 diphenhydramine, 5 other), and was not associated with decreased risk of ACVE, but was associated with increased risk of dysrhythmia (25% treated, 1% untreated, OR 19.5,  $p < 0.05$ ). Both dysrhythmias in the bicarbonate group occurred in patients with prolonged QTc (> 460 ms), and in long QT subgroup analysis, 40% of patients treated of bicarbonate developed dysrhythmia ( $p < 0.10$ ). **Conclusion:** Although underpowered to show benefit to prevent ACVE, there was a significant correlation with ventricular dysrhythmia in bicarbonate-treated patients with long QTc. This possibly results from bicarbonate-induced hypokalemia worsening QTc prolongation thereby increasing dysrhythmia vulnerability. Although further study is required we recommend close observation of QTc and electrolytes when bicarbonate is administered.

### 340. Clinical Experience of Prolonged Hypotension Following Combined Amlodipine and Direct Vasodilators Ingestion

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**Objective:** Overdose with the calcium channel blocker amlodipine can cause profound hypotension that may be exacerbated by the concurrent ingestion of

other antihypertensive agents. We report the clinical outcome of an overdose of amlodipine and direct vasodilators improving with the administration of hyperinsulinemic euglycemia therapy (HET). *Case report:* A 47-year-old woman presented to the emergency department 4 hours after a suicidal ingestion of two handfuls of amlodipine and direct vasodilators. Physical examination revealed lethargy but no focal neurologic deficit. The direct vasodilators were nicorandil and isosorbide dinitrate that were prescribed for her husband. Initial vital signs were: blood pressure 70/40 mm Hg; heart rate, 56 beats per minute; respiratory rate, 20 breaths per minute; temperature, 97.88°F (36.6°C). ECG demonstrated a sinus bradycardia, with normal PR and QRS intervals. Initial therapy included boluses of crystalloids, calcium chloride, and intravenous infusions of dopamine and norepinephrine which resulted in transient improvement in systolic blood pressure to 98 mmHg. One hour after her initial hypotensive episode, the patient suffered hypotension which was refractory to crystalloids, calcium chloride, norepinephrine, and dopamine. HET (0.5 U/kg/hr for 24 hrs) was started, rapidly improving her hemodynamic status and allowing a progressive weaning of the administered inotropic drugs and vasopressors over the next 24 hours. After a complicated 1-week hospitalization, the patient was discharged to an inpatient psychiatric facility with complete recovery. *Conclusion:* Hyperglycemia may occur as calcium channel blockade inhibits insulin release. Multiple case reports describe beneficial effects of HET in amlodipine overdose. Insulin increases plasma levels of ionized calcium, improves the hyperglycemic acidotic state, improves myocardial utilization of carbohydrates, and exerts its own independent inotropic effect. Amlodipine overdose can induce hyperglycemia, resulting in lethal cardiogenic shock owing to the decreased calcium influx and weakened inotropic effect. Coingestants may increase the severity of the toxicity of amlodipine. HET should be considered as secondary line treatment of severe calcium channel blockers overdose, especially with coingestants. *Reference:* 1. Smith SW, Ferguson KL, Hoffman RS, et al. Prolonged severe hypotension following combined amlodipine and valsartan ingestion. *Clin Toxicol* 2008; 46:470–4.

### 341. Severe Overdose of Quetiapine Treated Successfully with Extracorporeal Life Support

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*Objective:* To report a case where extracorporeal circulatory support (ECCS) was used successfully in severe quetiapine overdose. Quetiapine is a second-generation antipsychotic drug, used mainly in the treatment of psychotic disorders. Overdose is associated with sedation, tachycardia and a prolonged QT-interval on the ECG. Cardiovascular symptoms are uncommon but in severe cases profound cardiovascular depression may occur. *Case report:* A 40-year-old woman was admitted to the emergency department (ED) with reduced consciousness apparently due to intoxication. She had a history of schizophrenia and was treated with 900 mg of quetiapine daily. In the ED she presented with immeasurable low blood pressure, irregular bradycardia, hypothermia and a Glasgow Coma Scale (GCS) of 8. An immunoassay

test for tricyclic antidepressive agents (TCA) was positive. Blood samples analyzed with liquid chromatography-mass spectrometry method (LC-MS) were negative for amitriptyline and nortriptyline, but revealed a peak identified as quetiapine. LC-MS did not show the presence of any drug other than quetiapine. A serum quetiapine level 24 hours after the patient arrived was 715 ng/mL, and dropped to 124 ng/mL the day after. Despite resuscitation with intravenous fluids, intensive vasopressor treatment and renal replacement therapy (CRRT) the patient's condition deteriorated. The patient was quickly moved to an intensive care unit (ICU) where extracorporeal circulatory support (ECCS) could be instituted. The patient subsequently recovered after four days in the ICU without any residual symptoms. *Conclusions:* Severe poisoning with quetiapine may imitate tricyclic antidepressant poisoning and drug screening methods may be falsely positive for TCA. In case of cardiovascular collapse due to quetiapine overdose ECCS may be life saving.

### 342. Comparison of Vasopressors versus Placebo in Beta Blocker Toxicity in a Porcine Model

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*Objective:* Vasopressors (VP) are a standard treatment in shock. Pharmacotherapy with VP seems a logical approach to increase hemodynamic parameters and improve survival. Recent research on poison induced cardiogenic shock (PICS) suggests VP may be ineffective or even possibly harmful. We studied the effect of high-dose insulin (HDI) versus vasopressin and epinephrine (V/E) to treat  $\beta$ -blocker toxicity in a porcine model.<sup>1</sup> This study did not include a placebo group and therefore couldn't address how V/E therapy compared to placebo. We recently completed a HDI dose response study.<sup>2</sup> The model and method for toxicity was identical in both studies. The objective is to determine if V/E vs placebo therapy increases mortality in PICS by comparing these two studies. *Methods:* Comparison of the mortality rate and cardiovascular parameters of the placebo group in the HDI dosing study to the V/E study group. *Results:* Mean arterial pressure (MAP) differed significantly between the V/E group and the placebo group (75.3 mm Hg vs 49 mm Hg;  $p = 0.001$ ). SVR was also statistically different between the V/E and placebo group (2046 vs 1263 dyne  $\times$  sec/ $\text{cm}^5$ ;  $p = 0.013$ ). These effects would be expected per the pharmacological action of V/E. There was no statistical difference detected in cardiac output (2.55 vs 2.80 L/min/ $\text{m}^2$ ;  $p = 0.525$ ). A striking difference in survival was observed between groups. All 5 pigs in the V/E study group died within 90 minutes. Only 2 out of 4 pigs given placebo died in the 360-minute study interval, with neither of these deaths occurring less than 220 minutes post-toxicity. A log-rank test showed a statistical difference in survival between the two cohorts ( $\chi^2 = 7.5$  on 1 df,  $p = 0.0062$ ). *Conclusion:* This comparison suggests VP may have an increased mortality as compared to placebo in PICS by  $\beta$ -blocker. Further studies are warranted to define the benefit of VP in PICS. *References:* 1. Holger JS, Engelbrekt KM, Fritzlär SJ, et al. Insulin versus vasopressin and epinephrine to treat beta-blocker toxicity. *Clin Toxicol (Phila)* 2007; 45:396–401. 2. Cole JB, Engelbrekt KM, Stellpflug SJ, et al. 10 U/kg/hr of HDI is Superior to 1 U/kg/hr in a blinded, randomized,

controlled trial in poison-induced cardiogenic shock. *Clin Toxicol* 2011; 49:515.

### 343. Lipid Emulsion in Treatment of Verapamil and Benzodiazepine Toxicity: Clinical Effects and Serum Concentrations

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*Objective:* Recent experimental studies and case reports have shown that intravenous lipid emulsion improves hemodynamics in severe verapamil toxicity. Two cases of mixed verapamil and benzodiazepine overdose treated with Intralipid are presented. *Case series:* Case 1. A 41-year-old woman attempted suicide by ingestion of 7.2 g of verapamil and 120 mg of bromazepam. One hour later, she presented with somnolence and without any cardiac disturbances. Despite the decontamination treatment (gastric lavage, activated charcoal, IV fluids), two hours post-admission the patient deteriorated with a severe hypotension and coma. Prior to Intralipid, the patient received intubation, ventilation, flumazenil, calcium, glucagon and dopamine. Case 2. A 38-year-old woman ingested 5.6 g of verapamil and 150 mg of diazepam. The vital signs on admission 3 hours post-ingestion included hypotension (50/20 mmHg) and bradycardia (52/min) with an escape cardiac rhythm by ECG. Before the Intralipid was administered, the patient remained hypotensive and anuric for eight hours in spite of treatment with calcium and dopamine. Because of poor response to the conventional therapy, both patients received 500 mL of 20% Intralipid. It resulted in normalization of blood pressure within 20 (Case 1) to 60 minutes (Case 2). Other cardiac and CNS signs of intoxication also improved. Serum drug concentrations were analyzed by LC-MS in both patients before and after Intralipid administration. The specimens obtained after Intralipid were analyzed twice, before and after lipid had been removed from the samples by ultracentrifugation. In Case 1 drug concentrations were, for verapamil 0.65, 0.63 and 0.42 and for bromazepam 1.33, 1.26 and 0.34 mg/L, respectively. In Case 2, concentrations of drugs were, for verapamil 0.69, 0.64 and 0.41, and for diazepam 0.42, 0.52 and 0.28, respectively. *Conclusion:* Clinical effects and analytical results in both cases supported the idea of decreasing the effects of lipophilic drug by shifting it into the extended lipid compartment.

### 344. Mono Exposures to Beta-Blockers Reported to the Poisons Information Centre Erfurt from 2001–2010

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*Objective:* The aim of the study was to get recent information on important characteristics of all mono beta-blocker exposures (MBBE) reported to the Poisons Information Centre (PIC) Erfurt over a ten year period. *Methods:* In a retrospective study we analysed the development of frequencies, circumstances of exposure, symptom severity, age groups, and substances involved

in all MBBE-related inquiries to the PIC Erfurt from the beginning of 2001 to the end 2010. **Results:** In total, 846 MBBE were registered. Although MBBE increased almost twofold from 69 in 2001 to 104 in 2010 their relative frequency compared to all exposures remained almost constant 0.5% (0.4–0.7%) over the same period. Age groups involved in MBBE were more often children 45.5% (toddlers 34.2%) and less frequently adults 54.1%, than in all exposures (children: 40.0% (toddlers 5.3%); adults 59.2%). The frequencies of accidental MBBE (45.0%) and all accidental exposures (44.9%) were the same while suicidal intention was more often observed in MBBE (44.2%) than in all exposures (36.1%). The ten beta-blockers most frequently involved in MBBE were also the ten most often prescribed ones in Germany with slight differences in the rank order. Symptom severity was: none to mild MBBE: 68.2%, all exposures 65.2%, moderate MBBE: 2.8%, all exposures: 7.3%, severe MBBE: 1.3%, all exposures: 3.5%, unknown MBBE 27.2%, all exposures: 23.9%, and fatal MBBE: 0.5%, all exposures 0.2%. Highest rates of moderate or severe symptoms were seen with sotalol (3/26; 11.5%), atenolol (2/40; 5.0%), and bisoprolol (6/225; 5.0%). Three of 4 fatal cases occurred in talinolol exposures (3/26; 11.5%) and one in metoprolol exposures (1/341; 0.3%). **Conclusion:** The observed rise in MBBE was probably caused by the simultaneous increase in all exposures registered by the PIC Erfurt from 2001 to 2010. The frequency of MBBE seems to be triggered by the prescription rate of beta-blockers. Lower rates of moderate and severe symptoms in mono beta-blocker exposures compared to all exposures could be caused by the higher proportion of toddlers in MBBE. Talinolol exposure resulted strikingly often in death.<sup>1</sup> **Reference:** 1. Hentschel H, Schweder R, Freitag B, et al. Talinolol poisoning. 1999. Available at [http://www.ggiz-erfurt.de/pdf/pub\\_1999\\_hentschel.pdf](http://www.ggiz-erfurt.de/pdf/pub_1999_hentschel.pdf) [accessed Nov 2011].

#### 345. Rapid Reversal of Prolonged Hemodynamic Collapse due to Multi-Drug Overdose Using Intravenous 20% Fat Emulsion

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**Objective:** Successful cases of intravenous 20% fat emulsion (IVFE) administration for lipophilic agent overdose with hemodynamic instability have been previously reported.<sup>1,2</sup> However, there remains little data for multi-drug overdose. Theoretical mechanisms for IVFE include drug sequestration, mass action, and ion channel activation. We demonstrate successful use of IVFE to resuscitate prolonged hemodynamic collapse following cardiac arrest due to multi-drug overdose of antipsychotics and antidepressants. **Case report:** A 29 year-old woman with depression, prior suicidal attempts and bipolar disorder presented to the emergency department (ED) following a multi-drug overdose. Emergency medical services (EMS) found the patient on the floor in pulseless electrical activity (PEA) arrest with empty bottles of quetiapine, desvenlafaxine, escitalopram, bupropion, and ibuprofen. EMS intubated the patient and initiated ACLS protocol, regaining her

pulse in 20 minutes. Upon ED arrival, vitals were: T 33.9 C, BP 43 mmHg/palpation, HR 125/minute, assisted ventilation, oxygen saturation 100%. Physical examination was remarkable for GCS 2T, fixed/dilated pupils, absent reflexes (corneal, gag, noxious stimuli), hypoactive bowel sounds, and cold/dry skin. Rest of the examination was unremarkable. Laboratory results revealed: pH 6.94, HCO<sub>3</sub> 13.1 mmol/L, lactate 11.1 mmol/L. Complete blood count, creatinine, hepatic function, ethanol, paracetamol, and salicylate concentrations were unremarkable. ECG demonstrated sinus tachycardia with QRS duration 112 milliseconds and QTc 411 milliseconds. Resuscitation started with crystalloid, norepinephrine and sodium bicarbonate infusions, with persistent hypotension to 72/41 mmHg. Thus IVFE was started at 1.5 mL/kg bolus and 0.25 mL/kg/min continuous drip. Hemodynamics rapidly improved after the initiation of IVFE. Norepinephrine drip was titrated off by 1.5 hours. After 2.5 hours, BP was 105/77 mmHg and IVFE was stopped. In the intensive care unit, the patient remained normotensive off vasopressors but patient was terminally extubated due to severe anoxic brain injury. **Conclusion:** Despite poor neurologic outcome, this case offers a clear demonstration of IVFE reversal of hemodynamic collapse following multi-drug overdose. IVFE may allow for resuscitation of severe multi-drug overdoses, and should not be reserved only for single-drug overdose of lipophilic agents. **References:** 1. Finn SD, Uncles DR, Willers J, et al. Early treatment of a quetiapine and sertraline overdose with Intralipid. *Anaesthesia* 2009; 64:191–4. 2. Hillyard SG, Barrera-Groba C, Tighe R. Intralipid reverses coma associated with zopiclone and venlafaxine overdose. *Eur J Anaesthesiol* 2010; 27:582–3.

#### 346. Massive Diphenhydramine Overdose Presenting with Seizures and Ventricular Tachycardia Rapidly Improved with Intralipid Therapy

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**Objective:** Diphenhydramine is reported to cause seizures and a wide complex tachycardia after large ingestions. We report a case of a massive diphenhydramine ingestion resulting in status epilepticus and ventricular tachycardia that rapidly improved after intralipid administration. **Case report:** A 30 y/o female presented with altered mental status after a presumed overdose following a fight. She was initially combative before becoming unresponsive. On presentation to the Emergency Department, her vitals were a heart rate (HR) of 137 bpm, respiratory rate of 24, and blood pressure (BP) of 145/89 mmHg. She appeared anticholinergic with dilated, nonreactive pupils; dry mouth and axilla; diminished bowel sounds; and a large amount of urine was obtained on catheterization. Shortly after arrival she went into status epilepticus requiring intubation; the seizures responded to multiple doses of lorazepam. She then developed hypotension and a wide complex tachycardia resistant to cardioversion and amiodarone. She briefly went into pulseless electrical activity (PEA) that responded to epinephrine (1 mg). Lidocaine (1.5 mg/kg bolus) and sodium bicarbonate (200 mEq) were administered; norepinephrine (60 micrograms/min) and vasopressin (0.04 U/min) infusions were

started but she remained hypotensive in a wide complex tachycardia. Intralipid therapy (1.5 mL/kg bolus followed by 0.25 mL/kg/min for 1 hour for total infusion of 1 liter) was initiated. Her vitals improved with a HR of 84 and BP of 129/78 and the norepinephrine and vasopressin infusions were quickly titrated down and discontinued over the next 2 hours. During this time, her brother arrived with an empty bottle of diphenhydramine (25 mg, 400 tablets). She remained hemodynamically stable and was extubated the next day. A serum diphenhydramine level was 19,000 ng/mL (range 100–1000); tricyclic antidepressant and other drug levels were negative. **Conclusion:** In large ingestions, diphenhydramine is reported to cause wide-complex dysrhythmias due to sodium channel blockade. Diphenhydramine is lipophilic and therefore cardiovascular dysfunction from large ingestions may be improved with intralipid therapy. This is the first report that the authors found in the scientific literature regarding successful intralipid therapy administered to a patient after an intentional ingestion of diphenhydramine.

#### 347. Oral Toxicity of Buflomedil – Results of a Multicenter/Multinational Retrospective Case Series

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**Objective:** Buflomedil is used for symptomatic treatment of peripheral arterial occlusive disease because of its alpha1-alpha2-adrenolytic, vasodilating properties. A company marketing buflomedil was required in 2009 to present a Risk-Benefit-Assessment and asked all Poisons Centres in Germany, Austria and Switzerland via the Society of Clinical Toxicology about their experience concerning human exposures. **Case series:** 87 cases reported until 31 October 2009 were collected retrospectively. Among these cases there were 51 acute oral intoxications without co-ingestion. **Results:** 75% (n = 38) were > 14 years (= adults), 25% (n = 13) < 14 years (= children). 1. Adults: Mean age was 38 years (range 14–83 years). Follow-up information was available in 24% (9/38). Symptoms most reported were seizures (n = 10), tachycardia (n = 8), nausea/vomiting (n = 8), CNS-depression (n = 7), hypotension (n = 6), tremor (n = 3), hypertension (n = 2) and cardio-respiratory arrest (n = 2) or ventricular tachycardia (n = 1). Symptoms began early (0.3–4 h after ingestion). Ingestion of 150–1200 mg led to no or mild symptoms (n = 7). Moderate intoxications were seen from 1.5–4.2 g (n = 14), often after > 3 g. Ingestion of 4.5–15 g (n = 13) often led to moderate and severe poisoning. A 19-year old woman died in a cardiac arrest after taking 4.5 g. Cardiopulmonary resuscitation was successful after ingestion of 15 g. 2. Children: 62% (8/13) of the cases were followed up. Toddlers were asymptomatic after ingestion of 150–450 mg (n = 4). After ingestion of 600 mg (n = 5) no or mild symptoms were seen. Unknown doses (n = 2) led to seizures or no symptoms. In patients 6–14 years one child (62 kg) developed moderate symptoms

(seizure) after ingestion of 6 g. Another one (52 kg, maximum dose 15 g) had a cardio-respiratory arrest but recovered. **Conclusion:** Leading symptoms were seizures, tachycardia, CNS-depression and hypotension. In this case series 10% (n = 4/40) of patients weighing > 50 kg suffered from cardio-respiratory arrest or malignant ventricular tachycardia; mortality rate was 2.5%. Lowest lethal dose in adults was 4.5 g and higher than reported previously in the literature (3 g)<sup>1</sup>. The toxicity in children cannot be assessed finally because of the low number of cases. **Reference:** 1. Athanasis S, Maravelias C, Michalodimitrakis M, et al. Buflomedil concentrations in blood and viscera in a case of fatal intoxication. *Clin Chem* 1984; 30:157.

#### 348. Methylene Blue for Refractory Hypotension in Cardiovascular Drug Overdose

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**Objective:** Cardiovascular medications are a leading class of drugs involved in fatal exposures reported to the American Association of Poison Control Centers (AAPCC). Although therapeutic interventions for beta-blocker and calcium channel blocker poisoning include glucagon, calcium, high-dose insulin euglycemia (HIE) therapy, vasopressors, and intravenous fat emulsion, many cases are refractory to these interventions. We report the successful reversal of refractory drug-induced shock with methylene blue administration. **Case report:** A 69 year-old woman with depression and hypertension presented to the emergency department (ED) with lethargy after ingesting unknown quantities of amlodipine, atenolol, and thioridazine. Her initial vital signs were: BP, 135/62 mmHg; HR, 50 beats/min; RR, 18 breaths/min; and glucose of 10.5 mmol/L. One hour later, her BP decreased to 67/40 mm Hg with pulse of 44 beats/min. The electrocardiogram showed sinus bradycardia with normal PR, QRS (83 milliseconds) and QT intervals. She received intravenous fluids, glucagon (6 mg), and calcium chloride (2 grams) without improvement. Over the next 6 hours, the patient required maximum doses of norepinephrine, dopamine, and vasopressin, and remained hypotensive. HIE was initiated but discontinued due to hypokalemia and recurrent non-ventricular tachycardia. Although transvenous pacing captured, there was no improvement in her blood pressure. Methylene blue was administered at an initial bolus dose of 1 mg/kg over 10 minutes and the systolic blood pressure rose to 100 mm Hg with a pulse of 70 beats/min (mean arterial pressure > 70). Two 5-hour continuous infusions of methylene blue (2 mg/kg/hr) were administered 8 hours apart during which time all vasopressors were titrated off. Patient recovered without further complications and was transferred to psychiatric service. **Conclusion:** Methylene blue has been used in other vasodilatory shock states such as sepsis and anaphylaxis.<sup>1,2</sup> The proposed mechanisms of action include scavenging nitric oxide and inhibition of both inducible nitric oxide synthase and guanylate cyclase.<sup>1</sup> Methylene blue administration may reverse refractory vasodilatory shock due to multi-drug overdose. **References:** 1. Jang DH, Nelson LS, Hoffman RS. Methylene blue in the treatment of refractory shock from an amlodipine overdose. *Ann*

*Emerg Med* 2011; 58:565–7. 2. Paciullo CA, McMahon Horner D, Hatton KW, et al. Methylene blue for the treatment of septic shock. *Pharmacotherapy* 2010; 30:702–15.

#### 349. Hypotension, Junctional Bradycardia, QTc Interval Prolongation and Renal Impairment Following Acute Overdose with Sitagliptin

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**Objective:** We describe a case of hypotension, junctional bradycardia, QTc interval prolongation and renal impairment following acute overdose with sitagliptin. **Case report:** An 88-year-old woman with a history of diabetes mellitus, hyperlipidaemia, hypertension, coronary heart disease and congestive heart failure attempted suicide by ingesting 80 tablets (8,000 mg) of sitagliptin. She developed dizziness and vomiting and was found lying conscious on the floor 6 hours later. On admission to hospital, she was found to have bradycardia (HR 49 bpm) and hypotension (BP 80/40 mmHg). She had renal impairment with mild metabolic acidosis (plasma sodium 142 mmol/L, potassium 4.4 mmol/L, urea 14.3 mmol/L, creatinine 126 µmol/L, pH 7.31, pCO<sub>2</sub> 4.6 kPa, pO<sub>2</sub> 5.0 kPa, actual bicarbonate 18 mmol/L, lactate 2.1 mmol/L). She had hyperglycaemia (plasma glucose 18.6 mmol/L). Plasma troponin T level was normal. ECG revealed junctional rhythm (HR 52 bpm) and QTc interval prolongation (496 ms). She was given intravenous fluids, dopamine infusion and subcutaneous insulin. Plasma creatinine peaked at 48 hours after the overdose (246 µmol/L) before gradual recovery to 129 µmol/L. Both the bradycardia and QTc interval prolongation also gradually recovered (heart rate 55 bpm, QTc 466 ms at 23 hours; heart rate 79 bpm, QTc 394 ms at 97 hours). Urine drug screen by LCMS revealed sitagliptin and its metabolites; beta-blockers and calcium-channel blockers were not present. **Conclusion:** Following an acute overdose with sitagliptin, hypotension, junctional bradycardia, QTc interval prolongation and renal impairment may occur. There have been post-marketing reports of acute renal failure following administration of sitagliptin at therapeutic doses, but causative relationship remains inconclusive.<sup>1</sup> Hypotension and mild prolongation of QTc interval had been reported with sitagliptin at therapeutic or supratherapeutic doses.<sup>2–3</sup> However, junctional bradycardia and significant QTc interval prolongation have not been reported in the literature. The mechanism for hypotension is related to inhibition of degradation of endogenous vasoactive peptides such as substance P. The mechanism for QTc interval prolongation is not clear. However, sitagliptin was shown to inhibit hERG current in a hERG channel assay at high concentrations (IC<sub>50</sub> > 100 folds human C<sub>max</sub> at maximally recommended dose of 100 mg/day sitagliptin). **References:** 1. Sitagliptin prescription information. Available at: [http://www.merck.com/product/usa/pi\\_circulars/j/jjanuvia/januvia\\_pi.pdf](http://www.merck.com/product/usa/pi_circulars/j/jjanuvia/januvia_pi.pdf). Retrieved online 4 July 2011. 2. Ogawa S, Ishiki M, Nako K, et al. Sitagliptin, a dipeptidyl peptidase-4 inhibitor, decreases systolic blood pressure in Japanese hypertensive patients with type 2 diabetes. *Tohoku J Exp Med* 2011; 223:133–5. 3. Bloomfield DM, Krishna R, Hreniuk D, et al. A thorough QTc study to assess the effect of sitagliptin, a DPP4 inhibitor, on ventricular repolarization in healthy subjects. *J Clin Pharmacol* 2009; 49:937–46.

#### 350. Stress Cardiomyopathy Induced by Acute Cocaine Toxicity

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**Objective:** Stress cardiomyopathy (SC), also known as Takotsubo cardiomyopathy or “broken heart syndrome,” is characterized by transient acute heart failure elicited by a stressful event. Increased catecholamines produce myocardial dysfunction and edema<sup>1</sup>, with characteristic apical wall ballooning. SC typically resolves over a period of days to weeks. Toxin-induced SC is rarely reported.<sup>1,2</sup> **Case report:** A 41 year-old man presented to the emergency department (ED) following cocaine use. His vital signs were: HR 175/min; BP 160/90 mmHg; core temperature 41.7°C. He was severely agitated, and multiple police officers were required to restrain him. En route to the hospital he became unresponsive, and he was intubated upon ED arrival for airway protection. The initial electrocardiogram showed sinus tachycardia, 0.5 mm ST segment elevations in the inferior leads, and 0.5 mm ST depressions in the lateral leads. His troponin on presentation was 12.9 ng/mL and urine toxicology confirmed recent cocaine use. An initial bedside echocardiogram revealed a left ventricular ejection fraction of 15% with apical akinesis and biventricular hypokinesis, inconsistent with coronary arterial perfusion distributions. The patient experienced multi-organ dysfunction, including delirium, rhabdomyolysis, hepatic injury, disseminated intravascular coagulation, and acute renal insufficiency. After one week of supportive care, a repeat echocardiogram showed a normal ejection fraction without wall motion abnormalities. His other end-organ injuries resolved, and he was discharged from the hospital two weeks after admission. **Conclusion:** Traditionally, cardiotoxicity from cocaine manifests as coronary artery vasoconstriction, myocardial infarction, or dysrhythmia, largely as a result of sympathomimetic or sodium-channel mediated effects. This patient’s clinical presentation was consistent with SC in the setting of heavy cocaine use, and the diagnosis was confirmed by characteristic serial echocardiograms. SC variants are well described and dysfunction may occur in left midventricular or basal segments or biventricularly.<sup>1</sup> Clinicians should consider SC in cocaine users presenting with acute heart failure. **References:** 1. Eitel I, von Knobelsdorff-Brenkenhoff F, Bernhardt P, et al. Clinical characteristics and cardiovascular magnetic resonance findings in stress (takotsubo) cardiomyopathy. *JAMA* 2011; 306:277–86. 2. Amariles P. A comprehensive literature search: drugs as possible triggers of Takotsubo cardiomyopathy. *Curr Clin Pharmacol* 2011; 6:1–11.

#### 351. Intravenous Lipid Therapy: A Systematic Review of Published Case Reports

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**Objective:** To review published clinical cases where intravenous lipid has been administered as a potential antidote. Local anaesthetic agents are capable of causing severe systemic toxicity. Systemic lipid infusion in animals minimises bupivacaine cardiotoxicity in a dose dependent manner.<sup>1</sup> Case reports indicate intravenous lipid administration may successfully resuscitate patients with systemic toxicity. This has led to speculation that lipid administration might also reduce cardio-

toxicity attributable to other drugs. *Methods:* PubMed search criteria were: {'intralipid' OR 'lipid emulsion' OR 'lipid therapy' OR 'lipid administration' OR 'fat emulsion' OR 'fat therapy' OR 'fat administration'} AND {'parenteral' OR 'intravenous' OR 'administration' OR 'administer' OR 'antidote' OR 'rescue' OR 'treatment' OR 'therapy'}, limited to English language. Abstracts from EAPCCT and NACCT meetings were also searched. *Results:* PubMed identified 399 papers; 140 were relevant to the topic including 38 clinical cases. A further 41 cases were identified from meeting abstracts, hence 79 cases in total. These

involved local anaesthetic agents in 23 and positive clinical improvement was reported in all 23 (100%), calcium channel blockers involved in 14 with improvement in 5 (36%), psychoactive drugs in 20 cases with improvement in 11 (55%), antiepileptic agents in 8 cases with improvement in 6 (75%), and other agents in 13 cases with improvement in 10 of these (77%). A positive response to lipid administration was reported in 48 of 69 (70%) that involved highly lipid soluble drugs, compared to 8 of 10 (80%) of cases involving drugs with low to moderate lipid solubility. In cases where a positive response was recorded, there tended

to be a dramatic clinical improvement within 10–20 minutes after lipid administration. *Conclusion:* Comparatively few published clinical data exist. Similar response rates between drugs with high or low lipid solubility and the rapid clinical response do not support the widely postulated 'lipid sink' and suggest that other mechanisms of action might be important. *Reference:* 1. Weinberg GL, VadeBoncouer T, Ramaraju GA, et al. Pretreatment or resuscitation with a lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats. *Anesthesiology* 1998; 88:1071–5.