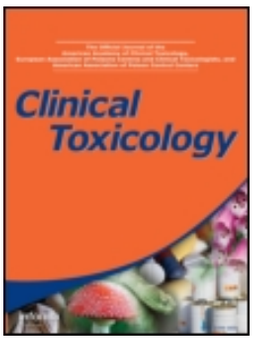

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ABSTRACTS

XXXIV International Congress of the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT) 27–30 May 2014, Brussels, Belgium

1. New insights in marine toxicology

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Introduction: Clinical marine toxicology is a rapidly changing area. The seas cover most of the surface of our planet with an enormous array of biotopes. Ignorance of the marine environment has made humans easy targets for the chemical weapons that sea creatures have developed in their intense struggle for survival. Indeed, many species have developed complex defence or attack systems involving not only sting apparatus but also production of toxic molecules as weapons. Man is only starting to understand this warfare and the variety of ways that marine species use toxins.

Discussion: Recent advances in the field of marine toxicology have been driven by two factors. The first factor is related to greater exposure of people in the northern hemisphere to the far greater potential toxic hazards found in the warmer seas of the southern hemisphere. Depletion of resources in cold and temperate waters has forced people who make a living from the sea to move into tropical waters to find what they can no longer have near to home. Similarly the increase in world travel associated with globalization has had the unexpected collateral effect of confronting European physicians with previously unknown toxic marine poisonings. The boom in exotic tourism over recent decades has been associated with an increase in the risk of poisoning and envenomation for European globetrotters. Global trade has also increased the danger of exposure to marine toxins. The sale of exotic foodstuffs has resulted in the occurrence of tropical food poisoning such as ciguatera and tetrodotoxism outside endemic areas. Severe envenomations have also been observed among owners of exotic venomous marine pets. The second factor is interest in global warming. Rising water temperatures and colonization of more and more territories by tropical species are tangible consequences of global warming. Since the Mediterranean Sea is a closed one, it is especially vulnerable to the effects of climate change and can serve as a sentinel of ecological disturbances (referred to as "tropicalization" of the Mediterranean by several authors) with the appearance of new toxic algae species and poisonous or venomous fish, within recent decades. Many of the new discoveries reported every year in Europe involve ecological disturbances that have induced modifications in the chorology, behavior, and toxicity of many species of venomous or poisonous aquatic life including algae (toxic blooms of dinoflagellates, but also toxic problems induced by macroalgae species), cnidarians, ascidians, fish, and shellfish.[1] These changes have raised a number of associated public issues.

Conclusion: The purpose of this review and synthesis of medical and scientific literature in marine toxicology is to highlight the growing challenges induced by ecological disturbances that confront clinical toxicologists during their everyday job in European Poison Centers.

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2. Neurotoxicity of 1-bromopropane in workers: An outbreak reported to the National Poison Center in Taiwan

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Background: 1-Bromopropane (1-BP, n-propylbromide), an alternative to ozone-depleting solvents, is used in degreasing, dry cleaning, spray adhesives, and aerosol solvents. 1-BP is a neurological and reproductive toxicant in animals and humans. Occupational exposure to 1-BP has been linked to adverse peripheral sensory, motor, and central nervous system effects. Here we report an outbreak of 1-BP-associated polyneuropathy in Taiwan.

Case series: We report a cohort of six cases of 1-bromopropane neurotoxicity occurring in a golf club cleansing factory. There were 1 male and 5 female patients ranging in age from 18 to 35 years with a mean of 28 years. They had been employed for 2.5–10 months. All patients had lower extremity pain, soreness or paresthesiae. Some of them complained of difficulty in walking (5), dizziness (4), nausea (4), fatigue (4), defecation difficulty (3), skin rash (3), back soreness (3), perineum/abdomen numbness (2), headache (1), and vomiting (1). On examination, some had sensory impairment (6), gait disturbance (5), spastic paraparesis (3), hyperreflexia (3), ankle clonus (1), and shortening of menstrual period (1). Urinary N-acetyl-S-(n-propyl)-L-cysteine (AcPrCys) was analysed and confirmed the 1-BP exposure in these patients with levels from 104.4 ng/mL to 2267.6 ng/mL. Neurophysiological examination revealed multiple conduction defects of the lower

limbs, abnormal vibration, abnormal visual evoked potential, and T2-weighted hyperintense lesions in the spinal cord; which is compatible with the diagnosis of toxic myelopathy or toxic polyneuropathy. Three patients are still under rehabilitation and have been unable to return to work 4 months later due to dominant neurological symptoms.
Conclusion: Using 1-BP as an alternative to ozone-depleting solvents causes a new form of occupational hazard. The pathogenesis of 1-BP has not yet been elucidated. For safety concerns, it is crucial to monitor the air level of 1-BP in the work place and urinary level of AcPrCys in workers.

3. Arthroprosthetic cobaltism: Clinical features, management and chelating therapy for a 2012–2013 case series from Pavia Poison Control Centre

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Objective. In recent years, safety concerns regarding metal on metal (MOM) hip prostheses have been raised.[1] Local and systemic toxicity associated with cobalt-chromium containing metal hip alloys have been reported. However toxicological evaluation and clinical management concerning hip surgical revision and chelation therapy are still debated.[2] We report clinical features, surgical and chelation therapy for a case series of patients referred to Pavia Poison Control Centre (PPC).
Methods: All patients with MOM hip prostheses referred to PPC from April, 2012 to August, 2013 were retrospectively reviewed. Patients were assessed for sex, age, type of prosthesis, cobalt and chromium whole blood levels, clinical manifestations and management.
Results: Twenty-one patients (mean age 62 years; 14 female) were studied. Type of hip prosthesis was characterized either by total (16/21) and resurfacing (5/21) systems. The manufacturer was known in 16 cases: De-Puy was the most represented (11) followed by Zimmer (2), Wright (1), Lima (1), and Stryker (1). Systemic toxic effects manifested in 4/21 patients with pericardial effusion (2 cases), heart failure associated with hearing-visual loss (1 case) and lower limb polyneuropathy (1 case). Time to onset of systemic manifestations ranged from 2 to 6 years from MOM implantation; in three patients abrasive local metallosis was evidenced. In one patient MOM system was implanted after ceramic hip prosthesis fracture. Cobalt and chromium blood levels ranged from 50 to 352.6 μg/L and 44 to 100 μg/L, respectively. All four patients underwent hip ceramic revision and metal levels normalized within 4–12 months after surgery. In one patient intravenous high dose chelation N-acetylcysteine was successfully administered for persisting high cobalt-chromium blood levels after surgical revision. In the remaining 17/21 cases no systemic toxic effects were reported and blood cobalt-chromium ranged 0.7–38 μg/L and 0.1–18 μg/L, respectively.
Conclusion: Arthroprosthetic cobaltism may result in neuropathy, cardiomyopathy, and hypothyroidism with late onset from prosthesis implantation. Clinical manifestations concerning prosthesis failure and/or systemic cobalt toxicity associated with rapid blood cobalt-chromium increase may represent key aspects either for surgical and toxicological follow-up and management of patients with MOM hip prosthesis.

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4. Computerized Early Warning System for emerging poisonings threatening public health

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Objective: In order to identify emerging poisonings at an early stage, a computerized Early Warning System (EWS) has been developed by the Dutch Poisons Information Center (DPIC). The first version was released in March 2013. Early detection is needed, for example, if exposure to a new product results in unexpected effects, if exposure to an existing product causes more toxicity than reported before, or if the number of poisonings with a certain product suddenly increases. The importance of using EWS is that these systems pick up signals in an early phase that otherwise might be missed by the staff of a poisons center.
Methods: The DPIC uses a computerized database (Toxicological Information and Knowledge system (TIK)) to register all information requests. Thereafter, for all products and/or compounds in TIK the number of registered information requests per product/compound is calculated. Based upon the number of requests in the previous 30 days and 3 years, two reference values are set. EWS compares the number of newly registered information requests at the end of every day to these reference values. All signals above the thresholds are listed and automatically sent by e-mail to the staff for further evaluation of the frequency, circumstances, and reported symptoms of these cases and exposures.
Results: EWS generates on a daily basis 0–8 new signals which need to be evaluated. Many signals are caused by seasonal related exposures (e.g., mushrooms, berries, carbon monoxide) or caused by a product that was recently entered into TIK and has no history of information inquiries. In June 2013 the EWS proved to be a very valuable tool. It generated a signal before an alert was given by one of the 24/7 poisons information specialists. This turned out to be a very serious signal regarding severe health effects following the use of a slimming product Dexaprine®. Shortly thereafter, Dexaprine® was withdrawn from the Dutch market.
Conclusion: The first experiences with EWS are promising for early detection of emerging poisonings threatening public health. Future evaluations will be carried out in order to re-evaluate

the set thresholds, for instance in better handling of seasonal influences.

5. Retrospective analysis of poisonings with newer psychotropic drugs

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Objective: To present a descriptive retrospective analysis of patients acutely intoxicated with newer psychotropic drugs treated in our toxicological department between 2000 and 2012.
Methods: Patients were included if they were symptomatic when admitted after an overdose with newer psychopharmaceuticals and ingestion was analytically confirmed. Only coingestion of ethanol and/or benzodiazepines was accepted. Less than six cases per substance lead to exclusion. The database search included the following groups of substances: selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), norepinephrine reuptake inhibitors (NRIs), monoamine oxidase inhibitors, tetracyclic antidepressants, atypical antipsychotics and anticonvulsants used as mood stabilizers. Severity of poisoning was estimated using the Poisoning Severity Score (PSS)
Results: 1111 drug poisonings were retrieved but only 74 (6.7%) fulfilled the inclusion criteria. The remaining drugs were: citalopram, mirtazapine, venlafaxine, clozapine, olanzapine, and quetiapine. Specific parameters for estimating the clinical severity of poisoning were: hypotension, central anticholinergic syndrome (CAS), cerebral seizures, and the duration of the in-hospital stay (see Table 1). Cardiac arrhythmias were not recognized. Worth mentioning was the prolongation of the QTc-interval that was most obvious in the citalopram group. Intubation was required in 21 (28.4%); gastric lavage was performed in 6 (8.1%); and activated charcoal was administered in 28 (37.8 %) cases. Specific treatment with sodium bicarbonate was performed in 7 (9.5%) cases due to QRS-prolongation and with magnesium in 4 (5.4%) cases due to QT-prolongation. Physostigmine was administered due to CAS in 7 (9.5%) patients. Intravenous lipid therapy was applied once. All patients survived.
Conclusion: Cerebral seizures, CAS, and hypotension were clinically the most relevant adverse events. The newer atypical antipsychotics were associated with a more severe clinical course of poisoning regarding the PSS.

6. Pregabalin: An assessment of its toxicity

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Objective: The aim of the study was to assess the toxicity of pregabalin in overdose, because there is little information in literature on this topic.
Methods: A multicenter retrospective analysis of cases of acute overdose of pregabalin. Inclusion criteria were monointoxication, defined dose, and documented follow-up. Severity of symptoms was assessed according to the Poisoning Severity Score.
Results: In total, 133 cases could be included. Patients involved were 21 children (0.06–13 years) and 112 adolescents (14–17 years) and adults (18–90 years). Doses ranged between 15–1350 mg (5.6–30.6 mg/kg) in children and 75–13,500 mg in adolescents/adults. More than half of the children (52%) remained asymptomatic, others developed only mild symptoms. In adolescents/adults 77% suffered from mild (63%) or moderate (14%) symptoms. Mild effects were observed from a dose of 75 mg (2.7 mg/kg) in children, whereas asymptomatic course was observed up to 300 mg (30.6 mg/kg). Doses from 225 mg and 200 mg caused mild or moderate symptoms in adolescents and adults, respectively. There were cases with a dose up to 4200 mg without symptoms. Two elderly people developed moderate symptoms at a dose of 75 mg. The clinical features of poisoning were particularly characterized by neurologic symptoms like fatigue (7%), drowsiness (7%), somnolence (26%), dizziness (12%), ataxia (10%), muscular symptoms like myoclonus (6%), and gastrointestinal symptoms (nausea/vomiting 9%). Infrequently, seizures,

Table 1. Parameters for estimating the clinical severity of poisoning.

Drug	Maximum serum level Mean [µg/L] (max./min.)	GCS Mean	PSS Mean	Tachycardia Heart rate > 100	Hypotension n RRsys < 100 MAP < 65	Anti-cholinergic syndrome n	Delirium n	Convulsion n	Days ICU Mean	Days until discharge Mean
Citalopram (n = 18)	1.786 (3.986/42)	11	2.13	11 (61%)	5 (28%)	3 (16.7%)	2 (11%)	5 (28%)	34	4.3
Clozapine (n = 11)	2.046 (4.910/75)	9	2.45	8 (73%)	4 (36%)	2 (18.2%)	6 (55%)	4 (36%)	51	5.5
Mirtazapine (n = 11)	1.848 (5.841/527)	12	2.10	8 (73%)	2 (18%)	1 (9.1%)	2 (18%)	1 (9%)	21	4.4
Olanzapine (n = 11)	703 (1.900/223)	8	2.55	9 (82%)	4 (36%)	1 (9.1%)	3 (27%)	1 (9%)	112	7.1
Quetiapine* (n = 15)	3.377 (10.450/74)	9	2.43	14 (93%)	4 (27%)	6 (40%)	4 (27%)	1 (7%)	53	9.1
Venlafaxine (n = 8)	4.364 (14.270/53)	14	2.38	5 (63%)	1 (13%)	1 (12.5%)	1 (13%)	5 (63%)	52	5.4
Total (n = 74)	2.335 (14.270/42)	10	2.33	55 (74%)	20 (27%)	14 (18.9%)	18 (24%)	17 (23%)	55	6.0

*Of 34 retrieved quetiapine cases, 19 had to be excluded as they were published previously.

tachycardia or bradycardia, hypertension, and respiratory insufficiency were observed.

Conclusion: In the present study, in most cases overdose of pregabalin resulted in no or only mild effects (88%). Only 12% of all patients suffered from moderate symptoms. Particularly, elderly people seem to be more susceptible. Severe symptoms were not observed. There is no clear correlation between dose and severity of symptoms. These findings are in accordance with the results of Lackey et al.[1] Further investigations are necessary to assess the toxicity of pregabalin especially in children.

Reference

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7. Are selective serotonin reuptake inhibitors responsible for an excess of morbidity in acute poisonings admitted to the emergency department?

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Objectives: Incidence of selective serotonin reuptake inhibitors (SSRI) in poisonings is growing. Their toxicity is considered low, but their actual impact remains unclear. Our objectives were to evaluate the consequences of SSRI exposures among poisoned patients admitted to the emergency department (ED).

Methods: We conducted a retrospective study including all poisonings involving at least one SSRI at a university hospital ED, from January 2009 to December 2012, matched with poisonings not including SSRI exposure, according to age, gender, type of drug, and ingested dose (after calculation of the dose equivalence for each pharmacological category); assessment of the impact of signs and symptoms of the serotonin syndrome was according to Sternbach's criteria[1] and Hunter's diagram.[2] Comparisons were performed using Chi-2 and non-parametric Mann–Whitney tests ($p < 0.05$). Data are expressed as median [25–75 percentiles] or percentage.

Results: In 4 years, 148 poisonings involving SSRI and 148 matched controls without SSRI were included. The involved SSRI included citalopram (36%), venlafaxine (20%), fluoxetine (19%), paroxetine (11%), and sertraline (7%). A serotonin syndrome was diagnosed in only one patient, but was actually present in four patients who had ingested SSRI, after proofreading their medical records. Twenty patients (14%) exhibited at least one serotonin syndrome criteria. Interestingly, at least 2/11 Sternbach's criteria and 2/9 Hunter's diagram criteria were systematically not assessed by the physicians in charge according to the patient's records. One venlafaxine-poisoned patient presented seizures and one citalopram-poisoned patient QT prolongation without clinical consequences. No cardiac failure or membrane-stabilizing effects were observed. Comparison between the two matched groups showed no significant differences regarding patient's outcome: lowest Glasgow score [14 (14–15) vs. 14 (14–15)], admission to the intensive care unit (5.4% vs. 4.3%), and hospitalization in a medical ward (8.0% vs. 7.6%).

Conclusion: Prognosis of SSRI-exposed patients is no different from prognosis of non-SSRI intoxicated patients admitted to the ED. Diagnosis of serotonin syndrome by the emergency physicians is still insufficient, justifying improved education and training.

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8. Seizures after single-agent overdose with pharmaceutical drugs: Analysis of cases reported to a poison center

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Objective: Occurrence of seizures after intoxications with pharmaceuticals is a well-known complication; however, only a few studies report on drugs commonly involved. In these studies, antidepressants were the most prevalent pharmaceuticals causing seizures and bupropion was the most common single agent involved. We analyzed the pharmaceuticals associated with occurrence of seizures after single-agent overdose and calculated the seizure potential of the most frequently involved medications.

Methods: A retrospective review of acute single-agent exposures to pharmaceuticals reported to the Swiss Toxicological Information Centre between January 1997 and December 2010 was conducted. Cases which resulted in at least one seizure were identified. Seizure potential of a drug was calculated by dividing the number of cases with seizures by the number of all cases recorded for that drug.

Results: 15,441 single-agent exposures to pharmaceuticals were reported. Seizures occurred in 313 cases. The study population consisted of 4005 patients 0–9-year old, 2573 patients 10–19-year old and 8349 patients $\geq$20-year old; age was not known in 514 cases. Seizures in these groups were recorded in 16, 95, 193, and 9 cases, respectively. The most prevalent drugs were mefenamic acid (51 of the 313 cases), citalopram (34), trimipramine (27), venlafaxine (23), tramadol (15), diphenhydramine (14), amitriptyline (12), carbamazepine (11), maprotiline (10), and quetiapine (10). Overall, antidepressants caused 136 of the cases. Drugs with a high seizure potential were bupropion 31.6% (6/19 cases), maprotiline 17.5% (10/57), venlafaxine 13.7% (23/168), citalopram 13.1% (34/259), mefenamic acid 10.9% (51/470), tramadol 9.6% (15/157), tolperisone 9.3% (5/54), trimipramine 8.0% (27/336), clomipramine 8.0% (4/50), and fluoxetine 7.6% (9/118).

Conclusion: Antidepressants play an important role in overdose-induced seizures. Other medications, such as mefenamic acid, an NSAID frequently used in Switzerland, are also a major cause. The most prevalent pharmaceuticals causing seizures do not necessarily have the highest seizure potential. This is shown for bupropion which has a high seizure potential, but was only involved in 2% of the cases with seizures, or for mefenamic acid which was the most

prevalent medication causing seizures, but ranked only fifth in the list of seizure potential.

9. Fatal salicylate levels can be lower than expected

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Introduction: Acetyl salicylate (ASA) poisoning is a common mode of self-harm in Western societies. Because hemodialysis is not recommended by many for the level alone until the ASA level exceeds 100 mg/dL, many may feel that serious ASA toxicity would not expected until the level is close to 100 mg/dL.
Objective: The purpose of this study was to describe the frequency distribution of ASA levels in fatal ASA poisonings.
Methods: Fatal poisonings reported to the American Association of Poison Control Center's (AAPCC) National Poison System Database (NPDS) from 2006 through 2011 were analyzed.
Results: In the 187 overall cases, the mean age ± SD was 47.6 ± 17.9 years; female sex 46%, male 54%; acute 130 (70%), acute on chronic 19 (10%), chronic 11 (6%), and unknown exposure 27 (14%); and relative contribution to fatality (RCF) I (undoubtedly responsible) 112, II (probably) 26 and III (contributory) 14 cases and 164 (88%) were intentional suicides. Overall, peak ASA levels ranged from 7 to 800 with mean/median of 92.9/91.3 mg/dL. In acute exposures the mean ASA was 100.5, acute on chronic 84.5 and chronic 46.5 mg/dL. In acute and acute on chronic exposures combined, the mean ASA level was 98.5 and lower 25% quartile was 78.5 mg/dL. In the undoubtedly and probably responsible categories combined, the mean ASA ± SD was 100 ± 69, median 96, and lower 25% quartile 77 mg/dL. Patients aged 50–79 years accounted for 33% of all poisoning deaths in NPDS for the latter 5 years with age available, but 41% of ASA fatalities.
Conclusion: ASA fatalities are usually the result of an intentional suicide act, and not limited to patients with very high ASA levels. Up to 25% may have a peak ASA level ≤77–78.5 mg/dL. Acute and acute on chronic fatal exposures have higher ASA levels than chronic exposures. ASA fatalities' age distribution is shifted toward an older age than all poisoning fatalities combined.

10. Visual damage after acute methanol poisoning: Prospective study in 50 patients

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Objective: To study long-term visual sequelae (VS) 4–8 months after acute methanol poisonings and the correlations with laboratory data, clinical symptoms, and treatment options.

Methods: Data were obtained from a prospective study in 50 patients with confirmed poisoning. Examination included standard ophthalmic tests, optical coherence tomography with retinal nerve fiber layer estimation (RNFL), visual evoked potentials (VEP), nuclear magnetic resonance imaging (NMRI). Admission protocols and discharge reports were collected during the outbreak in the Czech Republic in 2012. The variables were compared by unpaired Student's t-test. The exploratory factor analysis on Spearman and Pearson correlations between VS and variables studied was used.
Results: 41 males and 9 females, median age 48 (23–73) were examined. Median serum methanol on admission was 939 mg/L (85–7307), formate 578 mg/L (0–1400), pH 7.25 (6.69–7.46). VS were diagnosed based on both pathological retinal nerve fiber layer (RNFL) and visual evoked potentials (VEP) (latency P1 > 117 ms; amplitude < 3 mcV). VS were found in 40% of patients, including 8% with blindness. VS involved pathological complications: contrast sensitivity, color vision, perimetry, and fundoscopy (all $p < 0.01$). Only 55% of these patients had VS diagnosed at discharge in 2012. Patients with impaired RNFL had pathological VEP as well ($p = 0.011$). Sixty-eight per cent of patients with VS had central nervous system sequelae ($p < 0.001$), mainly symmetrical putamen necrosis. Patients with VS differed in methanol and formate level, pH, HCO_3^-, anion gap, base deficit on admission (all $p < 0.01$); no differences were found regarding age, gender, ethanol, pCO_2, glucose, lactate. Visual disturbances and coma on admission were more prevalent in patients with VS ($p = 0.012$ and 0.003, respectively). No correlation was found with the type of antidote ($p = 0.073$), folate treatment ($p = 0.838$), or mode of hemodialysis ($p = 0.672$). However, ethanol administration for first aid before diagnosis confirmation ($p = 0.0097$) negatively correlated with VS.
Conclusion: The number of VS was significantly underestimated in discharge reports. The damage occurred both in retinal nerve fibers and n.opticus. Damage of basal ganglia was present in 2/3 patients with VS. Neither folate substitution nor specific antidote (fomepizole) brought better outcome. Timely administration of ethanol in patients with suspicion of poisoning may prevent development of VS.

11. Intoxicated intensive care unit patients: Long-term mortality?

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Objective: The aim of this study was to use APACHE IV intoxication subgroups to assess and compare (case-mix adjusted) in-hospital and long-term mortality of intensive care unit (ICU) patients admitted with acute intoxication.

Methods: We linked a cohort of ICU admissions from a national ICU-registry (NICE, containing 85% of all Dutch ICUs) to records from an insurance-claims database. The cohort consisted of 7331 admissions between 1 January 2008 and 1 October 2011. Kaplan–Meier curves were used to compare the unadjusted mortality of the total intoxicated population and for specific intoxication subgroups based on the APACHE IV reasons for admission: (a) alcohol, (b) analgesics (aspirin, acetaminophen), (c) antidepressants (e.g., cyclic antidepressants, lithium), (d) street drugs (opiates, cocaine, amphetamine), (e) sedatives (hypnotics, antipsychotic, benzodiazepines), (f) poisoning due to carbon monoxide, arsenic or cyanide, (g) other toxins and (h) combinations of these diagnoses, maximum two. The diagnosis was based on clinical suspicion. The case-mix adjusted mortality was assessed by the odds ratio (OR) adjusted for age, gender, severity of illness, intubation status, recurrent intoxication, and several co-morbidities.
Results: The ICU mortality was 1.2%, the in-hospital mortality was 2.1%. The mortality at 1, 3, 6, 12, and 24 months after ICU admission was 2.8, 4.1, 5.2, 6.5, and 9.3%, respectively. Street drugs had the highest mortality 2 years after ICU admission (12.3%); a combination of different intoxications had the lowest mortality 2 years after ICU admission (6.3%). The adjusted observed mortality (ORadj) showed that intoxications with street drugs and "other toxins" have a significant higher mortality one month after ICU admission, ORadj = 1.63 and ORadj = 1.73, respectively. Intoxications with alcohol or antidepressants have a significant lower mortality one month after ICU admission (ORadj = 0.50 and ORadj = 0.46, respectively). The differences between these intoxications were not found in the adjusted mortality 3 months or more after ICU admission.
Conclusion: For intoxicated ICU patients, the difference between the in-hospital mortality and the mortality after 2 years is substantial (1.2% and 9.3% respectively). In the first 3 months after ICU admission there is a difference in mortality between some subgroups, however, this was not found after 3 months.

12. S100B protein predictive value for neuropsychological sequelae in carbon monoxide poisoning

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Objective: Carbon monoxide (CO) is the leading cause of poisoning-related deaths and 40% of survivors have delayed neuropsychological sequelae (DNS). DNS are more common in older and unconscious CO-poisoned patients and those having longer exposures to CO. Neurological scores and brain imaging might be useful predictors of DNS, but objectively a biochemical marker could be of great practical value. Serum S100B protein has already been shown to be a useful biochemical marker of brain injury. The aim was to evaluate the S100B protein as a prognostic parameter for late neuropsychological sequelae in CO poisoning.
Methods: In this prospective study we evaluated the clinical picture (consciousness level) and laboratory tests (carboxyhemoglobin, troponin I, creatine kinase, lactate, pH, and S100B levels) in CO-poisoned patients admitted to the emergency department in 2005–2010. The patients were treated with normobaric and hyperbaric oxygen if they had GCS < 15 or any other neurological deficits. At least 3 years later the patients were asked to fill out a questionnaire regarding headache, memory impairment, concentration problems, mood swings, and insomnia after CO poisoning. The Mann–Whitney test and logistic regression were used. A p value of < 0.05 was considered significant.
Results: 59 CO-poisoned patients were included. Only 20 returned completed questionnaires that were analyzed. On admission 40% of these patients had GCS < 15 and their mean carboxyhemoglobin level was 17%. They were treated with normobaric oxygen and 35% of them received hyperbaric oxygen too. No patient had any neurological deficit on discharge. The patients reported concentration problems (50%), memory impairment (45%), headache (40%), mood swings (35%), and insomnia (30%) developing a few days to weeks after discharge and lasting from several months up to 3 years. Serum S100B levels (μg/L) on admission were significantly higher in patients who reported concentration problems (0.16 ± 0.09), memory impairment (0.17 ± 0.09), headaches (0.17 ± 0.09), mood swings (0.18 ± 0.10) and insomnia (0.17 ± 0.11) compared to patients without sequelae (0.11 ± 0.10) ($p = 0.01$). Consciousness level on admission and other tested laboratory results did not correlate with all the evaluated DNS.
Conclusion: Serum S100B protein on admission is increased in patients developing concentration problems, memory impairment, headache, mood swings, and insomnia after acute CO poisoning.

13. Treatment of mustard gas poisoning: Results and long term consequences

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Background: The chemicals usually referred to as vesicants because of their ability to cause blistering of the skin are exemplified by bis-(2-chloroethyl)-sulfide or sulfur mustard (SM), commonly referred to as mustard gas. SM was first used in warfare on 12 July 1917 at Ypres and was estimated to produce a staggering 125,000 casualties on British forces alone before WWI ended in November 1918.[1] SM use since then includes Italy in Abyssinia in 1935–1940, Japan against China in 1937–1945 and most recently by Iran against Iraq in 1983–1988.[2] All the reports of SM clinical manifestations are very similar and well documented. If left untreated, SM injuries are very slow to heal taking, in some cases, many months and requiring a high level of nursing care.
Discussion: Sulfur mustard produces injuries to the skin, respiratory tract, gastrointestinal tract, and the eyes that have been likened to thermal burns or corrosive chemical damage, but there are some important differences in the pathology that have relevance to treatment strategies. Injuries are slower to develop than thermal burns, making maintenance of fluid balance less urgent. Unlike thermal burns where the inflammatory response is to the physical destruction of the tissues, SM produces an inflammation which precedes the tissue degradation, producing erythema, edema, and blistering of the skin.[3] Injury to the respiratory tract results in a dry, rasping cough and aphonia and airway epithelium becomes necrotic and sloughs off, destroying the mucocillary escalator and producing an increase in pneumonias. In the lower airways and the alveoli, damage to the epithelium and endothelium produces

a generalized pneumonitis and can lead to lung oedema. Later, pseudomembranes can be formed in the airways that can slough off and obstruct lower airways. The eyes respond in a similar way to the skin with a conjunctivitis possibly leading to blepharospasm and temporary blindness. Ulceration may result in bulbar perforation and possible permanent loss of sight.

The mechanism by which SM initiates tissue damage is not known. It is a bifunctional alkylating agent that produces cross linked DNA lesions that are difficult for the cell to repair and alkylates many proteins any one of which could lead to the massive inflammatory response observed. Lack of a defined mechanism of action has prevented the development of specific therapies so the treatment of SM injury is symptomatic and supportive. Skin injury is treated by excision of necrotic tissue on all but superficial wounds combined with appropriate post-surgical care. The best dressings are non-stick hydrogel/hydrofiber and there is some evidence that silver donating dressings produce better healing and there is some evidence that adjunct therapies such as ReCell that seeds the skin with autologous keratinocytes or the cosmaceutical nutrient mixture Aminoplex improve healing.[4] There is also evidence from experimental studies that early treatment with a combination of steroidal and non-steroidal anti-inflammatories may reduce the overall injury to the skin.[5] Treatment of eye injury is again symptomatic to relieve the irritation and pain associated with these injuries. Petroleum jelly on the margins of the eyelids will help prevent adhesions and in extreme cases homatropine eye drops may be beneficial, but the use of local anesthetics should be avoided. Injury to the respiratory tract is more difficult to treat requiring artificial ventilation in an intensive care environment in more severe cases. The removal of pseudo membranes by bronchoscopy and moist inhalation can be highly beneficial. Long term effects of SM can be debilitating. The skin may show hyper- or hypo-pigmentation and some scarring with recurrent blister formation on burn sites. Respiratory tract injury can produce a paroxysmal cough leading to sleep deprivation causing psychological problems. Commonly observed features of respiratory tract damage are dysphonia, chronic sinusitis, lower position larynx, limitation of vocal cords, mucosal inflammation of larynx, tracheobronchial stenosis, chronic obstructive respiratory disease, bronchiectasis, and fibrosis. Some of these symptoms may be relieved by N-acetylcysteine treatment, but the mechanism for this therapeutic effect remains to be established. Most patients with eye damage recover full sight but some severe cases may experience recurrent ulceration. A delayed corneal keratosis and persistent ulceration has been reported some years after the initial exposure.

The most serious long term effect of SM is cancer. As a bifunctional alkylating agent SM is a genotoxic carcinogen. There is much animal data to support this classification and epidemiological studies in workers from gas factories in WWII confirm the conclusion. SM is classified as a human carcinogen by the IARC.

Conclusion: Treatment of SM injury is supportive and symptomatic and severe cases require intensive care support and prolonged nursing care to achieve recovery. Recurrence of symptoms for many years after exposure are possible, the most serious of which include ulceration and keratosis of the eyes, obstructive pulmonary disease, lung fibrosis, and cancer. Drug therapies show promise but are not widely accepted or used. Future research using new methods (e.g., proteomics and genomics) may lead to an elucidation of the primary mechanism of SM cellular injury that might lead to more effective therapies.

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14. The art of poisoning: A history of toxicology through art and literature

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Background: Poisons and poisoning have always captivated the imagination of not only scientists, but also historians, artists, and storytellers. Art depicting poisoning comes in the form of paintings, detective novels, opera, and classic re-telling of history. Life imitates art when poisons are used in assassinations from espionage and political drama all the way down to the Lucrezia Borgias of domesticity. Poisoned artists also add to the melodrama of toxicology in the social consciousness.

Objective: To illustrate the history of toxicology through the various media in art and literature.

Methods: A comprehensive search of Google Scholar, LitMed, Embase, and art English-language databases was conducted to identify works of literature and art depicting poisoning. The bibliographies of historical texts were further reviewed for other relevant works

Results: Toxicology is predominantly represented in fictional literature, paintings, the opera, and film. Poisoning in history has remained the domain of female protagonists as their "weapon of choice". From Cleopatra's time to the Medici family's strong knowledge of toxicology to modern day fiction from Agatha Christie, poisoning is portrayed as an expedient tool of espionage, revenge and assassination plots. The majority of ancient poisons were derived from natural toxins, particularly herbs, flowering plants and seeds. Venomous animals, especially snakes, were both feared and venerated in art and literature from eastern and western cultures. These are typically depicted in Indian and Chinese art forms, such as classical dance and sculpture. The toxicology of the last millennium has progressed to the use of heavy metals, anti-cholinergics and purified toxins. Modern poisons in film and literature, such as cyanide, ricin and nerve agents, have evolved from natural sources into synthesized concoctions that rapidly "kill off" their victims.

Conclusion: Throughout history, humans have recorded the use of poisons in art and literature. The knowledge of alchemy, potions and chemicals has been portrayed as a dark force with practitioners feared for their "gift". The practice of clinical toxicology has much to learn from these history lessons.

15. Uridine triacetate: Antidote for 5-fluorouracil overexposure

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Background: 5-fluorouracil (5-FU) is broadly used to treat solid tumors. It is typically administered by intravenous infusion, at or near its maximum tolerated dose, over several days. Life-threatening or lethal 5-FU toxicity occurs due to errors in programming infusion pumps, infusion reservoir errors and dosage miscalculations. Patients with dihydropyrimidine dehydrogenase (DPD) deficiency (up to 3% of the population) leading to impaired 5-FU elimination also experience serious or lethal toxicity. In addition, some patients display unusual, severe, early-onset toxicities to 5-FU such as encephalopathy or cardiotoxicity, including cardiac arrest. Uridine triacetate is an orally bioavailable prodrug of uridine, the direct biochemical antagonist of 5-FU. Uridine triacetate has been used successfully to treat patients in emergency 5-FU overdose situations, patients with known or suspected overexposure due to DPD deficiency, and patients with 5-FU induced, sudden onset neurotoxicity and cardiotoxicity. More than 125 patients at excess risk of 5-FU toxicity due to overdose, accidental Xeloda (capecitabine) ingestion, possible DPD deficiency, or who displayed rapid onset of severe toxicities have been treated with uridine triacetate using a common treatment regimen and protocol.
Methods: Uridine triacetate was provided under emergency Investigational New Drug (IND) provisions or an expanded access protocol when requested by qualified clinical sites following 5-FU overexposures (most due to infusion pump errors) or early onset of severe toxicities. Patients received uridine triacetate (10 g every 6 h for 20 doses) as soon as possible after recognition of the overdose or possible clearance defect. Clinical outcomes, including safety, survival, and resumption of chemotherapy, were monitored.
Results: To date 125 patients overexposed to 5-FU have been treated with uridine triacetate. One hundred and twenty-two of these 125 patients recovered fully. Reductions in or absence of anticipated gastrointestinal, red hematologic, and other toxicities associated with 5-FU poisoning were observed, as well as rapid reversal of 5FU-induced encephalopathy and myocardial dysfunction. Mild or no adverse events were attributed to uridine triacetate.
Conclusion: Uridine triacetate appears to be a safe and effective life-saving antidote for 5-FU overexposure in emergency situations.

16. Pyridoxine is still useful in isoniazid poisoning?

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Objective: Acute isoniazid intoxication may require antidotal treatment with pyridoxine. In a survey aimed at evaluating antidote availability in the Italian National Health Service, pyridoxine was present in 30% of the emergency departments (ED). However, availability of intravenous pyridoxine formulation was interrupted in 2013 in Italy, and this aspect could complicate the hospitals' antidote supply. A retrospective analysis (2007–2012) of cases referred to Pavia-PCC was performed in order to evaluate the need for antidotal treatment in isoniazid poisoning.
Methods: All cases were assessed for: age, medical history, ingested dose, co-ingestants, accidental or intentional intoxication, clinical manifestations, treatment, availability of pyridoxine, and outcome.
Results: Twenty-seven patients (1–39 years; 33% ≤ 5 years) were included: group 1 – accidental poisoning 6/27 patients (1–36 years; dose ingested 8–20 mg/kg) and group 2 – intentional poisoning, 21 patients (78%; 12–39 years; dose ranging from 4 to 300 mg/kg, mean dose 74.25 ± 72.85 mg/kg). Co-ingestants (clarithromycin, paracetamol, fluoxetine, methadone, hyoscine, sobrerol) were reported in 7 cases of group 2. Major toxicity (seizures) manifested in 1/6 patients of group 1 and in 10/21 patients of group 2; seizures appeared within 2 h of ingestion in both groups. In total 20 patients (20/27; 74%) received antidotal treatment (in 9 cases as preventive treatment, before seizures appeared): pyridoxine was administered in 2 of group 1 in a dose of 3–7 g, and in 18 cases (86%) of group 2, in a dose of 1.2–15 g. Three patients of group 1 (3, 16 and 21-year-old) presented symptoms (vomiting and seizures) despite ingestion of a non-toxic dose (4–12 mg/kg).
Conclusion: Seizures frequently and rapidly complicate isoniazid poisoning, and for this reason treatment with pyridoxine should be started empirically even in an asymptomatic patient. In our experience some patients had symptoms in spite of a non-toxic dose ingested (history-based). Pyridoxine is an inexpensive and safe antidote that should be promptly available in adequate amounts in every ED.

17. Modified-release paracetamol (Panadol Osteo®) poisoning: Is the Australasian management guideline being followed?

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Background: The guideline for modified-release paracetamol (paracetamol-MR) poisoning in Australia recommends at least two serum paracetamol concentrations (serum[paracetamol]) 4 h apart to exclude toxicity and nomogram line-crossers. N-acetylcysteine (NAC) should be commenced with reported ingested doses > 200 mg/kg or 10 g, whichever is less, and stopped if two serum[paracetamol] are under the nomogram line.[1]
Objective: Describe a cohort of paracetamol-MR patients presenting to an urban hospital network and adherence to management recommendations.
Method: Paracetamol-MR cases identified from 921 patients presenting with paracetamol poisoning between October 2009 and September 2013. Data collected included demographics, paracetamol dose, serum concentration, N-acetylcysteine (NAC) treatment, alanine aminotransferase (ALT) and international normalized ratio (INR) results.
Results: There were 44 paracetamol-MR overdoses identified (68% female, median age 27 years) representing 4.7% of paracetamol poisoning cases. Deliberate self-poisoning in 42/44 (95%). NAC administered in 68% (n = 30). Median paracetamol-MR

dose-ingested 19,975 mg for NAC-treated vs. 7980 mg for non-treated ($p < 0.0001$). Median toxic initial serum[paracetamol] was 1145 μmol/L at 5.75 h post-ingestion. In 77% of NAC-treated patients initial paracetamol concentration was above the nomogram line. In 13% (n = 4) NAC-treated patients, initial serum [paracetamol] was non-toxic (median 502 μmol/L at 5 h) and subsequently crossed the nomogram line. One missed nomogram line-crossing patient had an initial non-toxic 4 h paracetamol (675 μmol/L) that was toxic (536 μmol/L) at 8 h post-ingestion. In 14 non-treated patients, initial median serum[paracetamol] was 497 μmol/L at 4 h. A second serum[paracetamol] was not measured in n = 8. Five of these reported ingesting more than 10 g and NAC was not initiated. Two patients had paracetamol-MR documented at triage but not noted by the treating doctor. There were no re-presentations with hepatotoxicity in non-treated patients.

Conclusion. In most cases, initial serum[paracetamol] indicated NAC treatment. However, there was a small number of nomogram line-crossers on second paracetamol measurement. Initial median serum[paracetamol] in treated line-crossers and non-toxic ingestions was similar, suggesting there may have been missed cases where serum[paracetamol] was not repeated. Observation of the guideline would have resulted in serial paracetamol estimation in all patients and based on ingested dose, at least five more patients treated with NAC ingested dose history.

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18. Effects of initial acetylcysteine infusion rates on adverse reactions in paracetamol overdose: A cohort study

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Objective: To determine whether rates of adverse reactions (ADRs) to acetylcysteine (NAC) are affected by prolonging the initial 150 mg/kg NAC infusion from 15 min to 1 h.

Methods: In September 2012 the UK Commission on Human Medicines (CHM) issued advice on the management of paracetamol poisoning, mandating the use of the "100 mg/L" line on all patients with paracetamol overdose, and of a 1 h, rather than 15 min NAC infusion. We used prospectively collected data for 12 months before (3 September 2011–2 September 2012) and after this (4 September 2012–3 September 2013) to examine the ADR rates to NAC, basing these on use and timing of "rescue medication" for emesis (antiemetics) or anaphylactoid symptoms (antihistamines and/or bronchodilators) or both. Patients in a concurrent clinical trial[1] were excluded from this analysis.

Results: No difference was noted in the overall incidence of adverse drug reactions to NAC overall before and after the CHM change [before 87/323 (26.9%) vs. after 145/514 (28.2%); absolute increase: 1.3%, 95% CI -4.9–7.5, p = 0.682]. There was also no change in the incidence of anaphylactoid reactions (AR) [before 29/321 (9.0%), after 55/514 (10.7%); absolute increase: 1.7%, 95% CI -2.4–5.8, p = 0.426]: or vomiting [pre 73 (22.9%), after 107 (20.8%) absolute decrease 2.1%, 95% CI 0.61–1.20, p = 0.367]. Admission paracetamol concentration < 100 mg/L had no effect on vomiting (OR 0.67, CI 0.43–1.05, p = 0.084), but anaphylactoid reactions were 5-fold less likely with admission paracetamol > 100 mg/L (OR 0.19, 95% CI 0.10–0.37, $p < 0.001$). Adverse reactions occurred later with a 1-hour (median 83.2 min, IQR 50–95) than a 15-minute infusion (47.5 min, IQR 20–50) (Wilcoxon rank-sum, $p < 0.001$).

Conclusion: Extending the time of the initial acetylcysteine infusion from 15 min to 1 h has no benefit on ADR profile, but results in later symptoms. As more patients with low paracetamol concentrations are now treated anaphylactoid reactions are likely to become a greater problem. We conclude that changing initial NAC infusions in current protocols from 15 min to 1 h offers no patient benefit.

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19. Use of artificial adaptive system software for real-time Poison Center outbreak localization

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Objective: Near real-time poison center data warehouses (PCDW) can provide outbreak situational awareness. Topological Weighted Centroid (TWC) is a mathematical model that is an intelligent, artificial adaptive system (AAS). This method utilizes the concepts of free energy and entropy – independent of call volume to identify the source and predict outbreak spread patterns from individual event geo-locations. We retrospectively applied TWC to analyze two separate outbreaks.

Methods: AAS software (Semeion Research Institute, Rome, IT) was used to analyze a 2001 Brazilian Dengue Fever outbreak from 54 municipalities in the State of São Paulo. Over a 5-month period, 10,676 cases were reported in seven 4-week data blocks. In the 2003 Colorado, US West Nile Virus (WNV) outbreak, 3688 dead bird locations from 22 July–4 September were analyzed to determine the outbreak's source. Only latitude and longitude were used for all TWC computations.

Results: Brazilian Dengue Fever source location: between São José do Rio Preto and Mirasol in the state of São Paulo. Disease spread: given only the data from the first (of 7) 4-week time periods, disease spread in the next time period was predicted and then from just the data given in the second time period, the movement of the disease was predicted for the next time period until the sixth time period predicted

the seventh time period. Findings were consistent with public health. Colorado WNV source location: from the total data set of dead birds, we focused only on those from the most severely affected area, yielding a data set of 96. The WNV source was shown to be located near Longmont, Colorado, US, consistent with public health findings.
Conclusion: Retrospective application of AAS software to geo-source data was correlated with traditional public health methods. AAS analysis can run in near real-time to augment public health investigations. Not only are infectious disease outbreaks amenable to AAS analysis but also other poison center calls such as drug exposures. Being a real-time system, an AAS could alert public health to an outbreak's source and evolving situational awareness pattern. We look toward continued exploration testing of these systems.

20. Using Twitter to measure underage alcohol usage

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Objectives: Underage alcohol use is a predictor of future risky behavior and mental and physical problems. National survey assessment of the extent of underage drinking is time-consuming, expensive, and prone to error, especially for illegal behaviors of minors who may not be forthcoming. We sought to investigate whether analysis of Twitter, a microblogging social network, would provide accurate estimation of the geographic distribution of underage drinking in the US.
Methods: We analyzed 4 months of data from Twitter's streaming Application Programming Interface for tweets that mentioned words related to alcohol consumption. We excluded tweets that only contained links to websites. All text was converted to lowercase, non-ASCII characters were ignored, stopwords were removed, and all words were converted to their dictionary form. A naive Bayes classifier (NBC), derived previously,[1] rated each tweet as "yes", "no", or "maybe", regarding likelihood of talking about alcohol usage. We then quantified alcohol usage in terms of two measurements we previously developed[1]: the Location Quotient (LQ) and the Risk Quotient (RQ). The LQ is ratio of "yes" tweets in a target query region to the fraction of "yes" tweets for a null query. The RQ is the number of users in a region whose fraction of "yes" tweets is greater than the 95th percentile for the nation. We compared geographic distributions of LQ/RQ with the gold standard, defined as the 2010 Substance Abuse & Mental Health Services Administration (SAMHSA) survey data for minors (aged 12–17) who consumed ≥ 1 alcoholic beverage/week across the continental US.
Results: To train our NBC, we used a curated data set of 5000 tweets. The inter-rater reliability for the curated data set was excellent (kappa = 0.87). LQ for underage alcohol tweets had excellent correlation ($R^2 = 0.94$, $p < 0.01$) with SAMHSA data. RQ identified areas of low-moderate risk, without significant state-by-state variation.
Conclusion. We successfully queried Twitter to accurately estimate the prevalence of underage alcohol usage with extremely high correlation to the US national survey gold standard. These data suggest that social media may be useful in supplementing epidemiological data in-between national surveys.

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21. Monitoring of domperidone and dextromethorphan intoxications reported to the Poisons Information Center following change in legal sales status

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Background: In the Netherlands the legal sales status of domperidone and dextromethorphan was changed from over-the-counter (OTC) "Pharmacy and Drugstore Only" to OTC "Pharmacy Only". This became effective in June 2009 for domperidone and in December 2010 for dextromethorphan. The motives for the change were different. For domperidone, an antiemetic, intervention of a pharmacist was considered to be essential to reduce life threatening interactions with other drugs that can cause cardiac dysrhythmias. Dextromethorphan, an antitussive, was mainly restricted because of its increasing abuse for psychotropic effects, often resulting in serious toxicity. Previous monitoring results of the National Poisons Information Center (NPIC) contributed to this status change. The effects of the change in legal sales status on the number of intoxications with domperidone and dextromethorphan reported to the NPIC were investigated.
Methods: The database of the NPIC was searched retrospectively for intoxications with domperidone and dextromethorphan before and after the status change for the period 2005–2012.
Results: The annual number of domperidone intoxications varied from 40 to 61 in the years 2005–2009. Since its new legal sales status took effect in June 2009, the number of intoxications did not decrease, with 65 in 2010, 53 in 2011 and 62 in 2012. For dextromethorphan a different picture was seen. From 2005 to 2007 the annual number of intoxications increased from 13 to 39, and stabilized until 2009. In 2010 there was a further increase to 70, especially in 13–17-year-olds (13 in 2009, 35 in 2010). After the new legal sales status was effective in December 2010, the number of intoxications sharply declined to 25 in 2011 and 20 in 2012. For the 13–17-year-olds the decrease was even more prominent, with 6 in 2011 and 1 in 2012.
Conclusion: The same change in legal sales status had a very different effect on the number of reported intoxications with domperidone and dextromethorphan. For domperidone no effect on the number of intoxications was observed. For dextromethorphan, however, the number of intoxications declined after the status change. Legal status change seems an effective measure to restrict abuse of dextromethorphan.

22. Acute poisoning in psychiatric patients

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Objective: There is a lack of prospective studies of poisonings comparing the pattern of poisonings between patients with and without a history of previous psychiatric illness. The aim of this study was to evaluate the frequency, intention and pattern of toxic agents in acutely poisoned patients with and without a previous history of mental disease.
Methods: A 1-year prospective, observational study of all acute poisonings in Yekaterinburg, Russia (population: 1,343,900, of whom 1,145,000 were ≥ 16 years). Patients ≥ 16 years of age who were in contact with any part of the health care system (ambulance service, hospitals, or the Forensic Institute) were included. The present material included only hospitalized patients.
Results: There were 1868 admissions to hospitals during the study. A psychiatric history was known in 1286 cases (69%), of whom 204 patients (16%) had a history of outpatient (59) or inpatient (145) psychiatric treatment. Females dominated among the psychiatric patients (57%, $p = 0.02$), but not among the rest (49%). A suicidal intention was recorded in 68% of the patients with a psychiatric history, compared to 47% among the rest. Repetitive suicidal attempts were found in 50% of the psychiatric patients and in 16% of the non-psychiatric patients. Neuroleptics and cyclic antidepressants were the most common toxic agents used for suicidal attempt by psychiatric patients ($p < 0.001$), whereas cardiac medication, paracetamol, and drotaverine dominated among the rest. Psychiatric patients showed a significantly higher level of suicidal intention according to the Beck scale in comparison with non-psychiatric patients (15 (8–19) and 6 (2–13), $p < 0.0001$).
Conclusion: There is a significant quantity of poisoned patients with mental disease. Intention and pattern of toxic agents involved in exposures are quite different from those in other patients.

23. Epidemiology and mortality of hospitalized acute poisonings in Yekaterinburg and Oslo: A comparison of two cities

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Objectives: Comparing poisoning epidemiology may be challenging due to differences in study design. We compare prospective data collected with the same study design covering two cities.
Methods: All acute poisonings in adults (≥ 16 years) presenting to a hospital in Oslo from April 2008 to April 2009 or in Yekaterinburg from March 2009 to March 2010 were included consecutively. A standardized form was completed by the treating physician covering the study aims.
Results: The incidence of hospitalized acute poisonings was 1.4 and 2.0 per 1000 in Yekaterinburg and Oslo, respectively. The most common toxic agents were ethanol (14% vs. 18% in Oslo) and benzodiazepines (9% vs. 15% in Oslo). In Oslo, a large proportion of poisonings were due to paracetamol or illicit drugs, whereas poisoning with cardiovascular drugs, neuroleptics, and antiepileptics were common in Yekaterinburg. The proportion presenting with a possible or definite suicidal intention was similar (47% vs. 46% in Oslo). The proportion with accidental drug overdoses was lower (11% vs. 37% in Oslo), while the proportion of other accidents was higher in Yekaterinburg (42% vs. 16% in Oslo). Interestingly, 1.1% of the poisonings in Yekaterinburg were classified as crimes. The inhospital mortality was 3.4% and 0.8% in Yekaterinburg and Oslo, respectively, while the proportion developing permanent sequelae was 0.7% and 0.5%.
Conclusion: The lower incidence of hospitalized acute poisonings and the higher mortality may indicate a higher threshold for hospitalization in Yekaterinburg. Furthermore, the proportion of accidental poisonings was higher in Yekaterinburg.

24. Impact of changes in UK management advice for paracetamol overdose on the numbers of adult patients admitted and treated in Newcastle upon Tyne?

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Objective: On 3 September 2012, the UK Medicines and Healthcare products Regulatory Agency (MHRA) recommended changes to paracetamol overdose management.[1] These included treating all patients with staggered overdose or doubt about ingestion time and lowering the treatment line to 100 mg/L at 4 h. This study was performed to quantify the impact of this change on paracetamol overdose management in Newcastle upon Tyne, UK.
Method: Retrospective review of all adult patients attending the emergency department between 2 September 2011 and 6 September 2013. The medical records of those with codes consistent with possible overdose were screened for paracetamol ingestion. Data was triangulated with plasma paracetamol concentrations, discharge summaries and the inpatient toxicology database to ensure that all patients were identified and duplicates excluded.
Results: Comparing the year before and after guidance change, the total number of patients presenting with paracetamol overdose and proportion admitted were not significantly different (Table 1). The proportion of patients treated with acetylcysteine increased from 29.6% (n = 119) to 42.2% (n = 181) after the change (OR 1.74, 95% CI 1.30–2.31; $p = 0.0002$).

Table 1. Impact of changes in UK management advice for paracetamol overdose on the numbers of adult patients admitted and treated in Newcastle upon Tyne.

Paracetamol overdose	Before	After	% Change
Patients discharged from ED	162	164	+ 1.2
Admitted for observation/ treatment	240	265	+ 10.4
Total attendances to RVI*	402	429	+ 6.7
Treated with acetylcysteine	119	181	+ 52.1

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Conclusion: Consistent with another published study,[2] guidance changes have increased use of acetylcysteine substantially.

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25. Etiology of severe acute fatal poisoning in southern Romania between 2004–2012

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Objective: To study the etiology and other characteristics of severe acute fatal poisoning in patients admitted to a pediatric poisoning department.
Methods: A retrospective study of severe fatal poisonings admitted to our department between 2004 and 2012 was performed. The following criteria were taken into consideration: age, type of poisoning, etiology.
Results: From a total of 69 deaths, the most common cause was carbon monoxide poisoning (23 cases). Other etiologies were noted: multidrug poisoning (9 cases), organophosphorus poisoning (9 cases), substance of abuse poisoning (8 cases), caustic poisoning (5 cases), hydrocarbon poisoning (3 cases), mushroom poisoning (3 cases), nitrite poisoning (2 cases), and one case each of intoxication with polyethylene glycol, methyl alcohol, Dentocalmin, aluminum phosphate, carbamazepine, and anesthetics. Regarding age, the majority of multidrug intoxications occurred in the age group 12–18 years and were severe voluntary intoxications. Substances most frequently involved were nonsteroidal anti-inflammatory drugs and various types of painkillers, oral antidiabetics, tricyclic antidepressants, benzodiazepines, and barbiturates. Acute intoxications with cholinesterase inhibitors have had two major etiologies: carbofuran and diazinon, and were mostly accidental poisonings. Among the substance of abuse poisonings, heroin was most commonly involved, followed by methadone, morphine and codeine. Among the caustic substances, caustic soda was the main cause of death, and for hydrocarbons, accidental diesel poisonings were the majority. The leading cause of death for patients under 12 years was acute carbon monoxide poisoning, followed by poisoning with cholinesterase inhibitors and caustics for the same age groups. For those older than 12 years we observed a predominance of multidrug acute poisoning deaths and substance abuse. Acute carbon monoxide poisoning was in third place.
Conclusion: Acute accidental carbon monoxide poisoning had the highest frequency in the etiology of poisoning deaths in the period 2004–2012, being the first cause of death due to poisoning at home. In our country, deaths due to heroin and methadone poisoning have become a reality.

26. Acute renal damage: Cause of death in acute severe poisoning in children

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Objective: To analyse the etiology and histological features of acute renal failure as the final stage of evolution in acute severe poisoning in patients admitted to a pediatric poisoning department.
Methods: A retrospective study of severe poisonings admitted to our department in a 9-year period (2004–2012) was performed. The following criteria were taken into consideration: presence of acute renal failure, etiology, histological findings.
Results: During this period 69 cases of deaths caused by acute poisoning were noted, of which, 20 patients (28%) had clinical and laboratory signs of acute renal failure.[1] In the etiology of toxic acute renal failure we identified the following: drug combinations 5 cases (25%), organophosphorus 4 cases; substances of abuse 3 cases; household substances 2 cases; Dentocalmin (local anesthetic containing lidocaine, formalin and menthol) 2 cases, mushrooms 2 cases, aluminum phosphate 1 case, methyl alcohol 1 case. Multidrug poisoning that evolved with acute renal failure involved the following combinations: nonsteroidal anti-inflammatory drugs and metamizol; colchicine and metamizol; oral antidiabetic (metformin) and metamizol; aminofenazone, caffeine and nifedipine; nonsteroidal anti-inflammatory drugs and carbamazepine. In all 20 cases, histologic confirmation of acute renal failure was made. The most commonly encountered aspect was acute tubular necrosis (10 cases), followed by tubulonephrosis (3 cases), interstitial nephritis (1 case), hidroprotidic dystrophy (1 case). The remaining 5 cases had nonspecific aspects of renal stasis. Most toxic substances analyzed in our study acted by direct toxicity, causing damage to the proximal tubule. In analyzing the etiology according to histology, we noted the association between multidrug and cholinesterase inhibitor poisoning and the appearance of acute tubular necrosis. Tubulonephrosis was identified in caustic poisoning and those that have evolved with cardiogenic or hemodynamic shock, as with Dentocalmin and carbamazepine.
Conclusion: Acute renal failure occurs immediately or in the evolution of acute, severe poisoning; the most frequent cause being the association of two or more drugs. Acute renal failure in acute severe poisoning is most commonly associated with acute tubular necrosis. Interstitial nephritis is rare in the pediatric population.

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27. Risks from Russia: An analysis of 225 intoxications with Russian medicines over a 15-year period

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Objective: There has been a close relationship between Russia and Germany for many centuries. After the fall of the Iron Curtain in the year 1989 many immigrants of German origin came from Russia to Western Europe. The immigrants often bring their medicines and sometimes use them in overdose. Hence there emerged

a new entity of intoxications with sometimes unfamiliar medicines. This can be a challenging situation for doctors and poisons centers. The objective of this analysis is to give an overview of the problem, identify the medicines involved, and describe the difficulties in identifying the substances.
Methods: Retrospective analysis of all cases of intoxications with Russian medicines in two poisons centers over a 15-year period concerning demographic data, the medicines, and the severity of the intoxications according to the poisoning severity score (PSS).
Results: From 1996 to 2010 the two poisons centers were consulted 225 times with regard to intoxications caused by medicines from Russia (GIZ-Nord: 189 cases, Zurich: 36 cases). PSS: 2 fatalities, 7 severe, 26 moderate intoxications; rest (n = 190) minor, asymptomatic or not documented. Two of the seven severe cases were due to drotaverine, a gastrointestinal spasmolytic agent with a putative anticholinergic effect. One fatal intoxication due to extreme hyperthermia was caused by dinitrophenol, a slimming medicine, licensed neither in Germany nor Switzerland. The mean age was 4 years for intoxicated children (n = 50) and 27.5 years for adults (n = 175).
Conclusion: Intoxications with medicines from Russia seem to be a relevant problem in Germany and Switzerland. There are a number of moderate, severe, and even fatal intoxications due to the involvement of sometimes not licensed substances with an unfavorable toxicological profile. Some basic knowledge of the Russian language, or at least the Cyrillic alphabet, can be helpful for the identification of the substances. In Russian, sometimes a Western H becomes a Russian G (Hamburg becomes Gamburg and Hannover Gannover). This knowledge was helpful in one difficult case when the poisons center was consulted for a geroin intoxication. This turned out be a heroin intoxication.

28. Evaluation of the completeness of epidemiological surveillance systems for poisoning by the capture-recapture system in Rabat and region, Morocco, 2012

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Objective: The main object of our study was to evaluate the completeness of the toxicovigilance system for epidemiological surveillance and its impact on public health as well as its ability to support decisions to define, develop and implement public policy intervention (control, prevention and care).
Methods: We used the capture-recapture method to estimate the number of missing cases and to adjust for undercounting to estimate accurately the number of poisoned people in Rabat and region in 2012.[1] We based this on the number derived from two regulatory systems, passive and exhaustive, of epidemiological surveillance: Poison Control and Pharmacovigilance Centre (PCPC) reporting form by mail and phone and emergency department records of provincial hospitals.
Results: Cases of poisoning by PCPC reporting forms and emergency department records in 2012 rose to 1058 and 836, respectively. One hundred and fifty-eight cases were found by both systems. After validating the conditions for the application of the capture-recapture method (in particular, having verified that the results from PCPC and emergency department were probably independent),[2] its utilization allowed us to evaluate the incidence of poisoning in Rabat and region in 2012 at 5598 cases. The calculated completeness values for PCPC and emergency department were 19% and 15%, respectively; 66% of cases were missed by both systems. This rate of completeness did not allow the PCPC to estimate the public health impact of poisoning. However, it allowed it to generate alerts, to support decisions to define, develop and implement public policy intervention.
Conclusion: These results show that it is difficult to evaluate the epidemiological importance of poisoning from the results of passive and exhaustive surveillance alone. The PCPC must establish a new surveillance system specific to each toxic substance. Moreover, it must advocate strengthening the regional dimension of poisoning surveillance in hospital networks and enhancing the role of public health services in the coordination of these networks. In addition, better education of health professionals on the importance of epidemiological surveillance would permit an improvement in the completeness of the results.

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29. Characterization of paracetamol overdose: Report of the Moroccan Poison Control Centre (2006–2011)

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Objective: Paracetamol is one of the most frequently used drugs in intentional overdoses in developed countries but paracetamol overdoses are rare in developing countries. We aimed to investigate the epidemiology and outcome of paracetamol overdoses occurring in Morocco.
Methods: Data for this study were extracted from the medical records of the Moroccan Poison Control Centre (CAPM). The center collects reports concerning poisoning cases from different regions of the country. A retrospective review of all reports received from 2006 to 2011, concerning acute paracetamol poisoning is described. The data included circumstances of poisoning, sex, age distribution, symptomatology, the outcome, the use of antidote and poisoning according to the year.
Results: Over 6 years, 319 inquiries involving acute paracetamol exposures were received at CAPM (3.2% of all drug poisoning cases received in this period). The female/male ratio was 1.5 and the largest age group was < 20 years (70.7%). The mean age

was 14.9 ± 4.2 years. 39.9% of the cases were suicide attempts, of which 81.8% were women, $p < 0.001$ (58.6% of cases were adults >20 years). Accidental exposures occurred mainly in boys (44.1%). Forty-two cases were medication errors. In 31.0% of the patients, the features were symptomatic (digestive symptoms in 66.7%) and considered to involve a hepatotoxic dose in 94 cases. 7.2% of patients required treatment with acetylcysteine. Only one patient died from acute hepatic failure.

Conclusion: Paracetamol poisoning is frequent despite the under-reporting of poisoning cases to the CAPM. Young women are the most affected in a suicidal context while boys are the most affected in accidental circumstances. The unavailability of plasma levels of paracetamol in different parts of Morocco except for the region of Rabat and of Fes (where toxicology laboratories are available) and the lack of a paracetamol poisoning treatment guideline minimize the use of N-acetylcysteine, which is available in Moroccan hospitals.

30. Morbidity and mortality associated with exposures to over-the-counter combination acetaminophen products in the United States

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Objective: Acetaminophen (paracetamol) is responsible for more exposures, as reported to poison centers, than any other substance. The literature is replete with publications that profile the demographics and outcome of those exposures. However, similar data are not as available for nonprescription products that contain acetaminophen in combination with other ingredients (e.g., antihistamines, cough suppressants). The purpose of this investigation is to characterize ingestions of nonprescription combination products that contain acetaminophen (paracetamol).

Methods: The American Association of Poison Control Centers National Poison Data System was queried over the period of 2000–2012 to identify all human exposures to acetaminophen-containing combination nonprescription products. The following demographics and exposure characteristics were analyzed: age, gender, exposure reason, site of care and medical outcome. Descriptive statistics were used to describe the data.

Results: A total of 643,197 human exposures that contained at least one acetaminophen-combination product were reported to American poison centers. Females accounted for 59.9% of the exposures. The mean age was 18.2 (SD ± 16.3) years and children ≤5 years of age were involved in 33.5% of the exposures; whereas, adults ≥60 years of age accounted for 2.0% of exposures. The most common reasons for exposure were: unintentional-general 34.0%, intentional-suspected suicide 32.1%, and intentional-therapeutic error 17.9%. The majority (47.7%) of the exposures were managed on site (e.g., non-health care venue-typically a residence), 18.0% were treated and released and 22.6% were admitted. Major morbidity outcomes occurred in 1.4% and there were 569 (0.1%) fatal outcomes. The number of reported exposures increased from 2000 (40,648) to 2008 (57,236) and declined steadily to 2012 (37,539). Exposure to a single substance was reported in 96.2%.

Conclusion: Acetaminophen-containing combination products are responsible for a significant number of exposures as reported to American poison centers. Young children account for a large number of the exposures. Morbidity and mortality is quite low.

31. Intentional substance exposures in young persons: Inquiries to the New Zealand Poisons Information Centre from 2008–2012

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Objective: To determine the epidemiology of intentional exposures in young persons reported to the New Zealand Poisons Information Centre.

Methods: Telephone inquiries involving intentional exposures occurring from 2008 to 2012 inclusive were reviewed. Patient demographics, product names and classifications, and treatment advice were collated and analysed.

Results: There were 107,090 poisoning cases, including 4804 self-poisonings where patient ages were recorded: 133 cases (2.8%) occurred in the 13-year-old group, 405 (8.4%) in the 15-year-old group, and 101 (2.1%) in the 24-year-old group. The 14–16-year-old group accounted for 1071 (22%) cases. At all ages (13–24 years) self-poisonings were more frequent in females (F/M = 1.50–2.89), and most marked in the 14–16-year-old group (F/M = 2.58–2.89), especially in cases involving pharmaceuticals (F/M = 3.76). Pharmaceuticals were most commonly involved (in 74.5 ± 5.1% of cases) at all ages. Analgesics (28.4% of cases) and anti-inflammatories (17.2%) were involved more commonly in the younger 14–16-year-old group than in the older 22–24-year-old group (18.7% and 10.4% of cases, respectively), whereas antidepressants (18.9%), antipsychotics (10.4%), and hypnosedatives (5.8%) were more common in the older than in the younger group (9.9%, 4.6%, and 2.6% of cases, respectively). Paracetamol (younger group 36.5%, older group 23.6% of cases), ibuprofen (16.3%, 10.6%), and codeine (8.4%, 7.6%) were common in both groups, whereas citalopram (older group 9.6%, younger group 4.6% of cases), quetiapine (6.9%, 3.4%), and zopiclone (6.3%, 2.4%) were more common in the older group. The proportion of cases requiring active medical investigation, treatment, or psychiatric assessment was similar for all ages (86.7 ± 3.3%) and correlated with the corresponding number of cases.

Conclusion: Paracetamol, ibuprofen and codeine analgesics were commonly reported in self-poisoning by young people in the 13–24-year-old age range. Prescription medicines citalopram, quetiapine, and zopiclone were involved more frequently in older than younger groups. The study suggests that easily accessible over-the-counter (OTC) analgesics and commonly prescribed antidepressants, antipsychotics and hypnosedatives are a ready means of attempted self-harm in young people in New Zealand.

32. Acute fatalities reported to the National Poisons Information Centre of Ireland from 2000 to 2012: A prospective observational study

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Objective: To describe the characteristics of acute poisoning fatalities reported to the National Poisons Information Centre (NPIC) of Ireland.
Methods: A prospective observational study was carried out from 1 January 2000 to 31 December 2012 inclusive using standardized data collected on consecutive cases reported to the NPIC. Potentially serious poisoning cases were routinely followed up by telephone to determine patient outcome; namely, recovery, sequelae or fatal. Data on patient age, gender, poisoning agent(s), signs and symptoms reported, cause of death where known, and the time of death (days) from when the NPIC was first contacted regarding the cases were collated.
Results: Over the 13-year study period, the NPIC was consulted about 151 suspected poisoning cases that subsequently had a fatal outcome. There were 146 fatalities in adults patients (aged > 14 years old) and 5 pediatric fatalities. The male–female ratio was 1.4:1. The mean age for adult females was 49 years and 45 years for adult males. The principal agents implicated in fatal cases were pharmaceuticals (n = 75, 49.67%), agrochemicals (n = 36, 23.84%), drugs of abuse (n = 20, 13.25%), industrial agents (n = 9, 5.96%), unknown agents (n = 7, 4.63%), household products (n = 3, 1.99%) and 1 cosmetic agent (0.66%). Paraquat poisoning was implicated in 21.19% (n = 32) of fatalities. The predominant pharmaceuticals involved were paracetamol (n = 13), venlafaxine (n = 10), propoxyphene/paracetamol (n = 9), verapamil (n = 5), and zopiclone (n = 5). Cocaine was the main drug of abuse and was implicated in 13 fatalities. The leading signs and symptoms reported for fatal cases were cardiac arrest (n = 57, 37.75%), acidosis (n = 36, 23.84%), hypotension (n = 36, 23.84%), coma (n = 30, 19.87%), and renal failure (n = 27, 17.88%). The leading causes of deaths were cardiac arrest (n = 51, 33.77%), brain death (n = 25, 16.56%), multi-organ failure (n = 24, 15.89%), unknown cause (n = 24, 15.89%) and respiratory failure (n = 9, 5.96%). The majority of patients died on the same day that the NPIC was contacted (n = 44, 29.14%), 23.18% (n = 35) died the following day and 29.14% (n = 44) died within 1 week.
Conclusion: Fatalities for poisoning cases reported to the NPIC were uncommon and were associated primarily with ingestion of pharmaceutical agents. Cardiac toxicity was the predominant clinical feature and the leading cause of death.

33. Enquiries to the National Poisons Information Centre, Dublin concerning new generation anticoagulant agents

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Objectives: New generation anticoagulant agents are increasingly being prescribed as an alternative to warfarin. Dabigatran (direct thrombin inhibitor) and rivaroxaban (Factor Xa inhibitor) were licensed in Ireland in 2008 with apixaban (Factor Xa inhibitor) being approved in 2011. The aim of this study was to characterize the epidemiology profile of enquiries about the new generation anticoagulant agents, dabigatran, rivaroxaban, and apixaban, to the National Poisons Information Centre (NPIC) of Ireland.
Methods: A retrospective review of telephone enquiries to the NPIC from 1 January 2008 to the 30 September 2013 was conducted. Enquiries relating to dabigatran and rivaroxaban, and apixaban were extracted from the NPIC database. Data on patient demographics, enquiry source, dose, symptoms, circumstances, and treatment recommended were collated.
Results: During the study period, there were 21 calls concerning 18 patients. Cases involved dabigatran (14 patients) and rivaroxaban (4 patients); there were no enquiries about apixaban. Cases involving dabigatran doubled over a 12-month period with 9 cases in 2013 compared to 4 cases in 2012. Seventeen enquiries involved adults ≥ 18 years (mean age 65; range 42–86 years) and there was one pediatric case (2 years old). Ten enquiries originated from general practitioner (GP)/GP Co-Ops, 5 from hospitals, 5 from community pharmacies and one from a member of public. Most cases involved therapeutic error (15 cases, 83%) and 40% of these cases occurred in patients under the age of 65. There were two intentional overdoses (11%) and one accidental ingestion (6%). In two cases, other drugs were co-ingested (one intentional overdose; one therapeutic error). Sixty-one per cent of patients were asymptomatic at the time of the call, two patients had neurological features and two patients had gastrointestinal features. Medical assessment was recommended in 72% of cases and 61% of patients required treatment in accident and emergency (A&E).
Conclusion: There was a dramatic increase in calls concerning dabigatran in 2013. This probably reflects the increased use of dabigatran as an alternative to warfarin. Most cases involved therapeutic errors and a significant percentage of these cases involved the under 65-year age group. This study highlights the need for healthcare professionals to provide clear instructions when prescribing new generation anticoagulation medication.

34. Analysis of the database of patients admitted with acute intoxications with substances of abuse in a large, university toxicology unit

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Objective: With thousands of patients dying from substance of abuse intoxication every day, the topic of overdose is a timely one. The aim of our study was to investigate the main demographic data, substances used and clinical outcomes of the patients presenting with substance of abuse acute intoxications in a large, university hospital.
Methods: This is a retrospective study of the database including all patients admitted to the toxicology unit with acute substance of abuse poisoning during 3 years (January 2010–December 2012), at the Emergency Hospital in Bucharest. We registered demographic data, substances of abuse used (single or in combination), motivation (i.e., suicidal or accidental ingestion), the clinical severity of poisoning using the Poison Severity Score and the main clinical outcomes (death, incidence and type of complications, intensive care unit and length of hospital stay).
Results: There were 3306 patients admitted with poisoning within the study period, with a male to female ratio of 1:1.2 (1467/1839). Of these, 688 cases of acute substance of abuse poisonings were recorded, accounting for 20.81% of the total number of poisonings. 78.6% of patients belonged to urban areas, 39.94% were unemployed and the patients were predominantly women (55.6%).

Overall, suicidal attempt (55.6%) was the predominant motivation. Male patients, aged 21–30 years, were predominant in the group with involuntary alcohol and opiate overdoses (73.26%), while women, aged 31–50 years, were predominant in the suicidal group (61.7%). According to the Poison Severity Score, the majority of these poisonings were minor (56.2%) and moderate (15.5%), while 24.8% were severe and the crude mortality rate was 2.3%. The most frequently involved substances were ethyl alcohol 17.15%, opiates 11.77%, psychoactive drugs 15.4%, benzodiazepines 14.53%, barbiturates 9.45%. Drug combinations were recorded in 28.4% of cases, while 6.11% were combinations of drugs and ethyl alcohol.
Conclusion: Our analysis shows the commonest profile of the patient presenting with acute substance of abuse poisoning is a female, aged between 31 and 50 years, who has ingested a combination of drugs with suicidal purpose. In the male group, the most common profile was accidental overdose of alcohol plus opiates.

35. Evolution of fatal cases by chemicals in the Spanish Toxic Surveillance System

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Objective: To follow the evolution of lethal cases by chemical products registered in the Spanish Toxic Surveillance System (STSS) since 1999. This STSS gathers acute poisonings by chemicals admitted to the emergency departments (ED) of Spanish hospitals. Since 1999 8931 cases have been collected from 20 hospitals.
Methods: Data are submitted by members of the staff of the ED of the hospitals involved in the program. The data file for each case includes: sex, age, symptoms, treatment, outcome, product identification, exposure cause, location of exposure, and exposure route. For the last 3 years an on-line form has been used for the collection of cases. Main chemical substances currently producing acute poisoning are: toxic gases (systemic and irritants), liquid caustics, solvents, pesticides, and detergents.
Results: There were 127 registered fatal cases, giving a mortality rate of 1.47% which is higher than the mortality rates of the total acute poisonings which is less than 0.5% in Spanish hospitals. Average age of lethal cases was 62 years, well above that found in overall chemical cases (39 years). Gender distribution of lethal cases was uneven: 63% males and 37% females, in contrast to the general group where the cases were evenly distributed. The type of poisoning was a suicide gesture in 87 cases (69%), domestic accidents in 28 cases (22%) and occupational accidents in 6 cases (5%). The mortality rate by chemical family was: pesticides 5.0%, caustics 2.0%, solvents 1.9% and toxic gases 0.8%. The mortality rates for the more dangerous agents were: carbon monoxide (CO) 0.86%, methanol 14.88%, hydrochloric acid (HCl) 20.22% and paraquat 44.20%. Only three paraquat cases, with one lethal, have been registered since the EU banning of this herbicide in 2007.
Conclusion: Poisoning by chemical agents shows a mortality rate higher than that for all poisoning cases. Lethal cases are more common in the older population and are mainly due to suicidal gestures. The most dangerous agents are paraquat, HCl, methanol, and CO. The EU regulation on paraquat has proved to be effective in preventing these most dangerous poisonings.

36. Fatal poisonings in the Toxicology Clinic of UMHATEM "N.I.Pirogov" for the period 2009–2011

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Objective: To study the hospital lethality from acute exogenous intoxications in the Toxicology Clinic, Department for Adults, of the Emergency University Hospital "N.I.Pirogov", Sofia, Bulgaria for the 3-year period 2009–2011.
Methods: The records of the Toxicology Clinic, Department for Adults, Emergency University Hospital "N.I.Pirogov" were reviewed retrospectively for all poisonings during a 3-year period, from 1 January 2009 to 31 December 2011. Fatal cases were analyzed with regard to gender, age and type of poisoning. The main reasons for the unfavorable outcome as well as the measures for diminishing hospital lethality are analyzed.
Results: A total of 2928 patients with acute poisoning were hospitalized in the Toxicology Clinic for the studied period, with fatal outcome for 44 patients. Hospital lethality was 1.50% for the studied period. In the separate years of the study it was respectively: 0.59% in 2009, 2.79% in 2010, 1.27% in 2011. Mortality was higher in men, 56.8% were males. Most deaths occur in the age group over 40 years, three quarters of patients with a fatal outcome (40–50 years 22.73%, followed by patients in the age group 60–70 years 18.18% and above 80 years 15.91%). The most frequent agents causing death were found to be toxic alcohols 34.09%, (methanol especially 25%), pharmaceutical agents 27.27%, corrosive substances 11.36%, others (carbon monoxide, opiates, *Amanita phalloides* mushrooms) 27.27%. The most frequently detected medicinal products in fatal poisonings were benzodiazepines, antidepressants, and antihypertensives; very often these were combined with alcohol.
Conclusion: The analysis of the data and the structure of the poisonings with fatal outcome revealed that for the studied period of time hospital lethality is a stable indicator with very little variation throughout the years. There was a clear relationship between a fatal outcome and a delay between ingestion and medical support.

37. Intentional self-poisoning by alkaline corrosive agents: A study for the period 2010–2012

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Objective: To present the results of a 3-year clinico-epidemiological study of features and severity of acute intentional self-poisoning by alkaline corrosive agents in the Toxicology Clinic, Emergency University Hospital "Pirogov", Sofia, Bulgaria. Attention was paid to the motivation of patients in carrying out the suicide attempt with corrosive agents.
Methods: The study included 43 patients with acute corrosive ingestion, hospitalized in the Toxicology Clinic for the period

1 January 2010 to 31 December 2012. Patient's motivation and mental disorders were investigated based on various psychological tests such as the Questionnaire for assessment of suicidal risk, the Hamilton Rating Scale for Depression and the Mini Mental State Examination (MMSE). The patients were followed-up with regard to general condition, local damage, psychiatric state, co-morbidity, and complications. Data were collected from clinical observations and examination, laboratory tests, imaging, and psychiatric tests.

Results: 43 patients between the ages of 22 and 82 with acute corrosive ingestions were observed. Eleven were male (25.6%) and 32 female (74.4%). All ingestions were intentional. Alkaline agents were used by all of the patients. The motivation in different age groups was also studied. The severity of poisonings varied from moderate to extremely severe. We observed a significant correlation between severity of intoxication and patient's motivation. Psychiatric co-morbidity occurred in patients such as depressive and schizoaffective disorder, as well as existential crises. Various complications were seen in 82% of the cases: severe bleeding, perforation, fistula or/and stricture formation. Two of the patients have undergone surgical intervention (coloesophagoplastic) and have recovered completely.

Conclusion: Acute corrosive ingestion of alkaline agents causes severe pathology. The severity and complex character of the injuries require good coordination between different specialists and a multidisciplinary approach to any patient with acute corrosive ingestion.

38. Patients presenting with acute poisoning to an outpatient emergency clinic in Oslo: A 1-year prospective observational study

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Objective: In Oslo, the majority of patients with acute poisoning present to and are treated in primary care, at an emergency outpatient clinic with limited diagnostic and treatment resources.[1] We describe the current poisoning panorama seen in this setting.

Methods: Observational study. Patients 12 years and older presenting to Oslo Emergency Outpatient Clinic (Oslo Legevakt) with acute poisoning were included prospectively from October 2011 through September 2012. Physicians and nurses registered data on preset forms. Main outcome measures were toxic agents, age, sex, intention behind the poisoning, referral, and time of presentation.

Results: There were 2923 episodes of acute poisoning in 2263 patients. Median age was 32 years, 1431 (63%) were males. The most frequent main toxic agents were ethanol 1400 (48%), heroin 490 (17%), benzodiazepines 201 (7%), fire smoke 191 (7%), and gamma-hydroxybutyrate (GHB) 115 (4%). In 902 (31%) poisonings there was more than one toxic agent, and the most common co-agents were benzodiazepines 320 (11%), ethanol 284 (10%) amphetamine 167 (6%), and cannabis/cannabinoids 113 (4%). In 493 episodes (17%), the patient was hospitalized, and in 60 episodes (2%) admitted to a psychiatric ward. Most poisonings (2328, 80%) were accidental overdoses with substances of abuse, 276 (9%) were considered suicide attempts, and the rest (312, 11%) were mere accidents. The male proportion among poisonings with illegal substances of abuse was 629/815 (77%), among ethanol poisonings 928/1400 (66%), among benzodiazepine poisonings 115/201 (57%), and among poisonings with pharmaceuticals (excluding benzodiazepines and legal opioids) 40/168 (24%). However, among the 452 ethanol poisonings in patients younger than 26 years, 222 (49%) were in females. Most of the young patients with ethanol poisoning presented during weekends (297, 66%), and among the weekend episodes 143 (48%) were in females.

Conclusion: The poisonings treated in primary care in Oslo are mostly due to accidental overdoses with ethanol or other substances of abuse. As in 2008,[1] about one in five were hospitalized. There appears to be a disconcerting weekend drinking pattern among adolescents and young adults, with young females presenting as often as young males with ethanol poisoning.

Reference

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39. Self-poisoning with drugs in Bamako, Mali

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Objective: Acute poisoning is a major public health issue in Mali. It constitutes a significant source of morbidity, mortality and health care expenditure. The aim of this study is to describe the main characteristics of drug self-poisoning as a pattern of acute poisoning in Bamako, Mali's capital.

Methods: This is a descriptive retrospective analysis of cases of intentional poisoning with drugs, reported between 2000 and 2010 in two University Hospitals (CHU) and six Health Reference Centers (HRC) in Bamako

Results: A total of 478 cases of self-poisoning with drugs were recorded between 2000 and 2010, constituting 75.6% of all cases of intentional poisoning reported in Bamako during this period. Of these, 406 (84.9%) patients were females and 80.7% were unmarried. Most victims were in their late teens or early twenties. Suicide attempts and self-induced abortion were the most common forms of self-poisoning (63% and 35% of cases, respectively). According to recorded data, the number of suicide attempts was 24 times higher than that for successful suicide. Women make 3.7 times more suicide attempts than men. The most commonly used drugs for self-poisoning were chloroquine (66.4%) and paracetamol (8.1%). On admission to hospital, patients received forced diuresis (76.6%), gastric lavage (64.7%), and induced emesis (20.2%). Among the 477 cases for whom the outcome was known, 21 (4.4%) of the patients died. For other cases, the outcome was favorable with or without sequelae.

Conclusion. Drug self-poisoning remains a major public health problem in Mali. The number of victims is probably underestimated because of undiagnosed and unreported cases.

40. Acute poisonings in Iceland: A prospective study of poisonings presenting to the emergency department at Landspitali University Hospital

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Objective: The purpose of the study was to assess the incidence and type of toxic exposures presenting to the emergency department at Landspitali University Hospital in Iceland. A nationwide prospective study carried out in Iceland during a 1-year period in 2001–2002 showed that 80% of all poisoning visits to medical care facilities in Iceland presented to the emergency department at Landspitali University hospital. A study of poisonings presenting to the University Hospital emergency department is therefore a good index of changes in pattern and incidence of poisonings in Iceland.
Methods: The study was prospective and included all visits due to poisoning or alleged poisoning to the emergency department at Landspitali University Hospital between 1 January, and 31 December, 2012. Hospital discharge records were reviewed and information collected included age and gender of each patient, previous poisoning history, time, location, causes and circumstances of the toxic exposure, type and amount of poison, route of exposure, clinical manifestations, treatment, outcome and length of stay in the emergency department.
Results: A total of 977 toxic exposures were documented representing an incidence of 3.1 cases per 1000 inhabitants per year. There were 554 females and 423 males; female to male ratio 1.31. The age range was from 2 months to 96 years. More than half of the patients were under 30 years of age. The majority of exposures occurred in the patient's home and ingestion was the most common route of exposure. Sixty-six per cent of all the poisonings were deliberate and 76% had drugs and/or alcohol as their main cause. Exposures to chemicals other than drugs were usually unintentional and 28% of them were occupational exposures.
Conclusion: Toxic exposures requiring emergency medical care are common in Iceland. Females outnumbered males. Self-poisonings by ingestion of prescription drugs and/or alcohol accounted for the majority of cases. The age range was wide, but the incidence was higher with young people.

41. Plasma pralidoxime concentrations: A paradigm in antidotal efficacy of pralidoxime towards paraoxon toxicity

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Objectives: A previous experimental study suggested a threshold of 4 mg/L for efficacy of pralidoxime (PRX) in cyclosarin toxicity. We looked at the concentration-dependence of efficacy of PRX in paraoxon (PO) toxicity in the rat.
Methods: Peristaltic iPrecio® pumps (Data Sciences, France) were subcutaneously (sc) inserted in male Sprague Dawley rats. Five groups (n = 5) were studied: PO received only PO (0.215 mg/kg, sc). PO+ PRX received PRX 30 min after PO to achieve steady-state concentrations of 4, 12, and 16 mg/L. The control PRX group received the highest dose resulting in concentration at steady state (Css) 16 mg/L without PO. The positive control group received PO only. Whole body plethysmography in awake rats was used and whole blood cholinesterase (WBChE) activity was measured.
Results: PRX alone at the Css 16 mg/L did not result in any significant clinical and respiratory effects. The PO dose resulted in overt SLUDGE (Salivation, Lacrimation, Urination, Defecation, Gastrointestinal distress and Emesis) toxicity from 30 to 240 min post injection and respiratory effects already reported. Residual WBChE activity was at 30%. Loading dose following by a continuous infusion resulted in steady state concentrations of PRX from 105 to 240 min post PRX injection. The Css 4 mg/L reversed neither clinical nor respiratory toxicity but resulted in significant increase in WBChE activity. The Css 12 mg/L partially reversed clinical signs, completely but transiently reversed respiratory toxicity. The Css 16 mg/L induced a complete and rapid reversal of clinical signs and respiratory toxicity.
Conclusion: These results are in close agreement with our previous results showing a significant, complete, albeit transient effect of a single intramuscular dose of PR in PO poisoned rats. The antidotal effects of PRX are strongly dependent on plasma concentrations in PO-poisoned rats. Without any additional atropine, the Css 4 mg/L significantly improved WBChE activity without clinical and respiratory toxicity. In contrast the Css 16 mg/L completely reversed the clinical and respiratory toxicity induced by a dose of PO corresponding to 50% of the median lethal dose. Further studies are needed to assess the concentration dependency of PRX at higher toxic doses of PO and other organophosphates.

42. Paracetamol poisoning in Melbourne, Australia: Are we maintaining the NAC of treating paracetamol poisoning?

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Background: An Australasian paracetamol poisoning guideline was released in 2008.[1] Specific recommendations include minimization of liver function tests (LFT) and international normalized ratio (INR) ordering in early presenters, commencing N-acetylcysteine (NAC) in late presenters before blood test results return and administering intravenous NAC loading-dose over 1 h to reduce histamine reactions.
Objective: Describe the epidemiology of paracetamol poisoning in an urban health care network. Assess compliance with above-mentioned aspects of the national guideline.
Method: Retrospective case series of paracetamol poisoning presenting to four emergency departments from October 2009 to

September 2013. Data included demographics, paracetamol formulation, dose and serum concentrations, treatment and adverse reactions to NAC, results and timing of LFTs and INRs.
Results: There were 921 presentations identified. Females 77%. Mean age 25.9 years. NAC was administered in 390 cases and 370 (95%) were deliberate self-poisoning (DSP). Median reported ingested dose was 18,000 mg (250 mg/kg) for NAC-treated vs. 7740 mg for non-treated DSP patients. Time to presentation for NAC: 74% less than 8 h (early) and 26% more than 8 h (late) post-ingestion. NAC administration was delayed while awaiting blood results in 30/97 (31%) of late presenters. Median NAC duration was 21 h (range 1–133 h). Adverse reactions to NAC: gastrointestinal reactions in 39%, histamine reactions 9.2%. Initial median paracetamol concentration was significantly lower with histamine reactions (644 vs. 922 μmol/L; $p = 0.0001$). Peak ALT was >1000 IU/L in 17/370 (4.6%) patients, three of whom were early presenters. There were no deaths or liver transplants. Of note, 89% of NAC-treated early presenters had at least two ALTs, 94% two INRs and 69% at least two paracetamol concentrations measured in the first 24 h.
Conclusion: Overall outcome was favorable in this cohort even though late presenters comprised 26% of cases and NAC administration was delayed for blood results in one-third of this group. Histamine reactions were in the lower range reported in the literature. To reduce the high frequency of repeated paracetamol, LFT and INR estimation in early presenters with a low risk of hepatotoxicity increased awareness of the guideline is required.

Reference

1. Daly FFS, Fountain JS, Murray L, et al. Guidelines for the management of paracetamol poisoning in Australia and New Zealand. Med J Aust 2008; 188:296–301.

43. A review of physical exam findings associated with anticholinergic poisoning reversed with physostigmine

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Objective: Physostigmine is a cholinergic agent that can safely and effectively reverse anticholinergic poisoning when used appropriately. Due to previous reports of complications, many clinicians are hesitant to utilize this agent as an antidote; only administering it when a "complete" anticholinergic toxidrome is present. This is particularly problematic when dealing with anticholinergic medications with multiple receptor affinities that elicit different exam findings than those associated with the standard anticholinergic toxidrome.[1] Our objective was to describe physical exam (PE) findings identified in a cohort of patients treated successfully with physostigmine for the reversal of anticholinergic poisoning.
Methods: Retrospective chart review of all patients treated with physostigmine by a toxicology consult service at a large academic medical center 1 January 2011–31 October 2013. Data collection included information on agents ingested as well as mental status and PE findings in successful reversals.
Results: 57 cases were given physostigmine during the reviewed period; 46 cases had obvious anticholinergic reversal. Anticholinergic medications ingested included diphenhydramine, hydroxyzine, quetiapine, cyclobenzaprine, clozapine, trihexyphenidyl, benztropine, perphenazine, prochlorperazine, promethazine, Donnatal (belladonna alkaloids and phenobarbital), and olanzapine. Primary mental status findings were coma/somnolence in 25/46 (54%) and agitation/delirium in 21/46 (46%). Hallucinations or picking behavior was noted in 31/46 (67%). PE findings included: 15/46 (33%) with mydriasis, 37/46 (80%) with tachycardia, 5/46 (11%) with temperature over 38°C, 15/46 (33%) with flushing, 37/46 (80%) with dry skin, 40/46 (87%) with dry mucous membranes, 37/46 (80%) with decreased or absent bowel sounds, and 31/46 (67%) had documented urinary retention.
Discussion: Although toxidromes can be useful in establishing a differential in unknown poisonings, oft-cited PE findings are not always present after exposure. All patients in our cohort had some degree of mental status impairment. Other common findings included tachycardia, dry skin, dry mucous membranes, and hypoactive bowel sounds. Unreliable exam findings included pupil size, temperature, and skin flushing.
Conclusion: Physostigmine administration should be based on the entire clinical picture rather than the presence of all findings associated with the anticholinergic toxidrome.

Reference

1. Richelson E. Receptor pharmacology of neuroleptics: relation to clinical effects. J Clin Psychiatry 1999; 60 Suppl 10:5–14.

44. Rivastigmine toxicity safely treated with pralidoxime without atropine

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Objective: Rivastigmine is a carbamate cholinesterase inhibitor formulated as a matrix patch and indicated for the treatment of mild to moderate dementia associated with Alzheimer's and Parkinson's Disease. In the setting of overdose, signs and symptoms of cholinergic toxicity are expected. We hypothesize that when indications for treatment with atropine are not met, pralidoxime (2-PAM) alone may be safe and effective at treating nicotinic effects and shortening hospital lengths of stay.
Case report: A 76-year-old man with Parkinson's Disease (PD) and hypertension applied 40 rivastigmine 13.3 mg/24 h patches dermally at bedtime. Approximately 5 h later, the patient awoke with severe tremulousness, blurred vision, salivation, lacrimation, diffuse muscle aches and extremity weakness. His wife removed the patches at home and called 911. In the emergency department, the patient's vital signs were: blood pressure 175/74 mmHg; heart rate 62/min; respiratory rate 16/min; oxygen saturation 100%; and temperature of 36.7ºC. On examination, he exhibited lacrimation and salivation, significant resting tremor, and 2/5 strength in both upper and lower extremities. He did not have bronchorrhea or decreased respiratory effort. The patient's skin was thoroughly cleansed,

intravenous (IV) hydration was started and he was admitted to the hospital. Twelve hours from the onset of symptoms, the patient's profound extremity weakness did not improve. Pralidoxime 1 g IV was slowly administered over 30 min, with an improvement in motor strength testing from 2/5 to 3/5 in both upper and lower extremities shortly after drug administration. His weakness and tremulousness continued to resolve and he was transferred to a skilled nursing facility on hospital day 6.
Conclusion: While the clinical effects of medicinal carbamate toxicity are often self-limited, prolonged nicotinic effects may occur in significant overdose with a dermal reservoir. Animal and human data provide support for the safety of 2-PAM with atropine in carbamate toxicity. Additionally, case reports, such as this one, suggest that 2-PAM without atropine may be safe and effective in patients with medicinal carbamate toxicity and only nicotinic symptoms.[1]

Reference

1. Hoffman RS, Manini AF, Russell-Haders AL, et al. Use of pralidoxime without atropine in rivastigmine (carbamate) toxicity. Hum Exp Toxicol 2009; 28:599–602.

45. A Belgian survey on the management of acute paracetamol intoxications by emergency physicians

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Objective: How uniform is the treatment policy for acute paracetamol poisoning in a country with a low incidence of paracetamol poisoning.
Methods: A survey was sent by e-mail to 482 emergency physicians in different types of hospitals. They were asked to answer questions on a hypothetical adult patient presenting at the emergency department (ED) 2 h after a paracetamol overdose. The answers were given by multiple choice and/or free text. They were specifically asked to react as they would do with a real patient including getting information from external sources
Results: We received 97 answers (20%), a low number which could be explained by the time of year (sent in July) and by dealing with physicians with a lack of time. The responses were predominantly from general hospitals (74), the remainder from university hospitals. To the question regarding from which dose in mg/kg the intake is considered as toxic the answers were 50 mg (5 answers), 75 mg (14), 100 mg (24), 125 mg (4). Which total dose taken do you consider toxic, received answers from 4 to 14 g, with predominance of 6 g (13 answers), 8 g (29), and 10 g (23). If a blood level is known, from which level do you start N-acetylcysteine? The answers were 50 mg/mL (9 answers), 75 mg/mL (3), 100 mg/mL (12), 150 mg/mL (28), 200 mg/mL (10), and 250 mg/mL (0). Risk factors were considered by 73 of the 97 respondents. If the intake was considered as possibly toxic what actions should be taken? They could choose one or more of the following answers: gastric lavage, charcoal, immediate administration of acetylcysteine, immediate paracetamol level, paracetamol level 4 h after intake and contact the Poison Centre. The most chosen combinations were: charcoal/acetylcysteine/level 4 h (20 answers), charcoal/acetylcysteine/immediate level/level 4 h (11), acetylcysteine/level 4 h (11), and charcoal/level 4 h (9). The choice of only a level at 4 h was chosen by three physicians. Gastric lavage (alone or in combination) was chosen by 12 physicians.
Conclusion: There is no uniform approach in Belgian hospitals for handling paracetamol intoxications. Some actions like gastric lavage, charcoal more than 2 h after intake and a paracetamol level 2 h after intake are not in line with existing guidelines.

46. Hydroxocobalamin: An antidote for sodium azide poisoning?

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Objectives: Sodium azide (NaN_3, CAS 26628-22-8) is a highly toxic inorganic compound. The mechanism of toxicity is not fully understood, but an interference with oxidative phosphorylation may be supposed. Poisonings with sodium azide are very rare and accordingly admissions to hospitals are even more uncommon, because most persons ingesting a significant amount of sodium azide are found dead or in problematic conditions, due to the fast onset of life-threatening symptoms. Despite the very high toxicity of sodium azide, an algorithm for effective treatment of such intoxications is lacking. Experimental tests and some case reports suggest a therapeutic effect of antidotes for cyanide poisoning, although the effectiveness of amyl nitrite, sodium nitrite or sodium thiosulphate could not be proved in severe intoxications with sodium azide.
Case report: A 25-year-old female laboratory assistant ingested a spoonful of sodium azide with suicidal intention. The patient developed severe hypotension, coma, and lactic acidosis. Despite treatment with catecholamines in an intensive care unit her condition changed to a critical state. Therefore, considering the data published about the possible effectiveness of antidotes for cyanide poisoning, it was decided to administer hydroxocobalamin, which led to a rapid improvement of the circulatory insufficiency. She could be discharged from hospital in a good condition.
Conclusion: While the mode of action of hydroxocobalamin in this case is not clear yet, an interaction with nitrogen oxide is considered to be a possible mechanism. Cyanide poisoning could be excluded by laboratory testing, but hydrazoic acid could be detected. The improvement of the patient's condition was quite impressive, but no other case of poisoning with sodium azide treated with hydroxocobalamin could be found in the literature. Concerning the poor outcome using the other antidotes for cyanide poisoning the usage of hydroxocobalamin in severe intoxications with sodium azide should be taken into consideration.

47. Successful use of fomepizole during second trimester of pregnancy

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Objective: To report a use of fomepizole during second trimester of pregnancy.
Case report: A 26-year-old female, 16 weeks pregnant, presented to the emergency department 5 h post-ingestion of 200 mL of concentrated ethylene glycol. She presented with general malaise and was found to have a metabolic acidosis (pH 7.31, bicarbonate 10 mmol/L, pO_2 16.0 kPa, pCO_2 2.7 kPa, base excess −14.0 mmol/L). Admission blood results were not available to calculate the osmolar and anion gaps; subsequent results at approximately 4 h post-ingestion showed a normal anion gap of 12.2. Her plasma osmolarity, however, was 315 mOsm/kg, with a suggested osmolar gap of 32 mOsm/L. An ethylene glycol concentration of 2500 mg/L was later confirmed. There have been no studies on the safety of fomepizole in human pregnancy and therefore the risks posed to the fetus are unknown. Fomepizole has been used in pregnancy without adverse effects.[1] The National Poisons Information Service (NPIS) may advise treating pregnant patients with fomepizole as opposed to ethanol which is contraindicated in pregnancy. In this case, it was suggested that if the osmolar gap was found to be raised, fomepizole should be administered, with consideration given for the role of hemodialysis. Ethanol was not recommended due to the known teratogenic effects. Follow-up of the patient revealed that she was treated with an initial dose of 720 mg of fomepizole and a further dose of 480 mg 12 h later. The patient made a complete recovery and was discharged on day four. The pregnancy continued uneventfully to full term, no abnormalities or complications were noted. The baby required a brief stay in the Special Care Baby Unit for an unassociated mild hypothermia.
Conclusion: Use of fomepizole to treat ethylene glycol poisoning during the second trimester of pregnancy was not associated with any adverse effects.

Reference

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48. Poisonings in Greenland: Remote-area challenges

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Objective: Treatment and monitoring of poisoned patients in resource-limited areas might be challenging when treatment guidelines are targeted at high-tech societies. We report the status of inquiries from Greenland to the Danish Poison Information Center (DPIC). We further identify areas with technological challenges in relation to current treatment guidelines, and discuss alternative treatment decisions based on the available antidote supply and facilities in the remote-areas of Greenland.
Methods: Inquiries from health personnel and citizens in Greenland were collected from August 2006-November 2013. The inquiries were divided into 18 main groups, and further evaluated in sub-groups based on the possible need for specific antidote treatment. The most severe sub-group subjects are presented here.
Results: DPIC received 434 inquiries regarding a total of 416 exposures. In the main group of alcohols (15%) the subgroup toxic alcohols represented 2%. Paracetamol represented 16%, iron containing vitamins 12%, and digoxin 1% of all inquiries. As for antidotal therapy, sparse laboratory facilities and unavailable xenobiotic concentration measurements formed the main challenges. Antidote preparedness demanded selected antidotes be readily available at all medical facilities. However, high costs and short shelf-life challenged the purchase of some essential antidotes. Severe poisonings with toxic alcohols, paracetamol, iron, and digoxin represented potential demands for specific antidotes and non-available advanced treatment modalities. Alternative low-tech treatment and monitoring needed to be implemented in potentially severe poisonings: toxic alcohols – unavailability of specific antidote fomepizole and serum-ethanol. Alternative treatment was intravenous ethanol, dosed by calculated maintenance dose and monitoring for acidosis using urinary pH and respiratory frequency; paracetamol – unavailable serum-paracetamol. Alternative treatment was antidote N-acetylcysteine dosed using standard of care treatment guidelines; iron – unavailable serum-iron and blood-gas analysis. Alternative treatment was antidote initiation in symptomatic patients and timed sequential urine monitoring of reddish-brown urine color complex formed by chelation of free iron and deferoxamine until clinical improvement and no further changes in urine color; digoxin – unavailable serum-digoxin and specific antidote. Alternative treatment was multiple-dose activated charcoal and electrocardiogram (ECG) guided dosing of atropine and lidocaine.
Conclusion: A qualified treatment of severely poisoned patients in remote/resource-limited areas is possible based on the combination of a limited antidote selection and basic clinical monitoring.

49. Five years of antivenom delivery: Cooperation between the National Serum Depot and the Dutch Poisons Information Center

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Background: Since spring 2008, a National Serum Depot (at RIVM) is operational in the Netherlands, guaranteeing rapid antivenom supply for the treatment of venomous bite and sting victims. The National Poisons Information Center advises on the contents of antivenom available in the Depot, and on the antivenom delivery to physicians treating these medical emergencies.
Methods: A retrospective analysis from April 2008 to April 2013 of the Poisons Center database. Information requests concerning exotic, venomous bites and stings and antivenom deliveries were analysed.
Results: 26 incidents involving exotic, venomous snakes were registered. In 81% the snake belonged to the Viperidae and in 19% to the Elapidae. All but one of the adult victims were males. Twenty-five victims were bitten in the upper extremities and one was spit in his eye. At least two patients were bitten 4 times at different time points in this 5-year period. Antivenom stored at the National Serum Depot was delivered in 12 cases, and in 8 cases antivenom

was administered to the patient. Antivenom indication criteria were the severity of the local effects and coagulation disorders. Fifteen information requests were related to scorpion stings. Eleven incidents took place in the Netherlands and included three children (7–12 years) and two teenagers (16–17 years). The incidents involved six terrarium scorpions and five stowaways, three of them were found in suitcases after returning from a holiday and two scorpions were encountered at the workplace. In six cases, identification of the, at first unidentified scorpion was possible, four *Centruroides* spp, one *Euscorpius italicus,* and one *Androctonus* spp. None of the incidents resulted in serious signs and symptoms and no antivenom was delivered. The remaining four information requests were related to sting incidents outside The Netherlands. All these victims were adults. No serious bite incidents by venomous spiders occurred.

Conclusion: A National Serum Depot with antivenoms to treat venomous bites and stings by exotic animals, especially snakes, is necessary in a Western European country. The cooperation with the Poisons Information Center guarantees information on antivenom availability and on the correct antivenom to be administered.

50. Hydroxocobalamin administration falsely lowers carboxyhemoglobin determination

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Objective: Carbon monoxide poisoning is a leading cause of mortality in the United States and other developed countries. In the setting of a house fire with a concomitant concern for cyanide toxicity, the New York Fire Department has a standing protocol that includes the administration of hydroxocobalamin. *In vitro* evidence suggests that the bright red color of hydroxocobalamin may cause interference with spectrophotometric laboratory tests. Although of concern, case reports demonstrating this interference are sparse. We report a confirmed discrepancy between carboxyhemoglobin determinations made on clinical specimens taken before and after hydroxocobalamin administration.

Case report: A 13-year-old girl was found unresponsive with no burns in a house-fire. Upon emergency medical service (EMS) arrival, the patient was intubated for airway protection and was administered hydroxocobalamin. By protocol emergency medical services (EMS) obtained blood specimens prior to hydroxocobalamin administration. Her vital signs in the emergency department were: blood pressure, 128/78 mmHg; heart rate, 78/min; intubated; temperature, afebrile. Blood drawn at hospital presentation revealed a carboxyhemoglobin of 6.6%. Subsequent analysis of the blood obtained by EMS prior to hydroxocobalamin administration revealed a carboxyhemoglobin of 23.9%. The patient received 4 h of hyperbaric therapy. She was extubated 2 days later and was noted to have a normal neurological examination. The cooximeter used was Rapid Lab 1265 for both specimens.

Conclusion: Caution is advised in the interpretation of any colorimetric testing following hydroxocobalamin administration and a high suspicion for carbon monoxide poisoning should be maintained. Blood drawn by pre-hospital providers should be analyzed to ensure an accurate percentage of carbon monoxide.

51. L-carnitine supplementation in the treatment of acute valproic acid overdoses

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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. Manifestations of acute valproic acid toxicity reflect both exaggerated therapeutic effects and impaired intermediary metabolism.[1] Central nervous system depression is the most common finding, although rarely hepatotoxicity and hyperammonemia have been reported in the acute overdose setting. L-carnitine is an amino acid derivative that is an essential cofactor in the β-oxidation of fatty acids. A few observations suggest that L-carnitine supplementation may increase the β-oxidation of VPA, thereby limiting cytosolic ω-oxidation and the production of toxic metabolites that are involved in liver toxicity and ammonia accumulation.[2]

Case series: From January 2011 to September 2013, 21 patients with acute VPA intoxication were admitted to our Clinical Toxicology Unit. In addition to gastrointestinal decontamination and supportive management, 9 patients required L-carnitine supplementation due to hyperammonemia or severe intoxication (VPA plasma level $>$450 mg/L or reported ingestion of more than 400 mg/kg). All patients were treated with loading dose of 100 mg/kg intravenously (up to 6 g) over 30 min, followed by 15 mg/kg every 4 h over 10–30 min.[3] No side effects were observed. Median length of hospital stay was 6 days and within the fourth day ammonia and VPA plasma levels went back in range. One patient reported life threatening cardiac arrhythmias probably sustained by VPA induced quinidine-like effect and needed temporary intracavitary cardiac pacing. None of our patients experienced any sequelae.

Conclusions: Our experience shows that early parenteral L-carnitine supplementation speeds up the decrease of ammonia and VPA plasma levels in acute poisoning. The lack of significant adverse effects and the relatively affordable cost strongly suggest the use of L-carnitine in severe VPA poisoning, in order to treat or even prevent hyperammonemia and improve clinical outcome.

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52. Factors associated with prehospital naloxone use in the United States: 2010

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Objectives: (1) Describe prehospital use of naloxone in the United States (US) in 2010. (2) Identify county level emergency medical services (EMS) and sociodemographic predictors of prehospital naloxone use. (3) Generate profiles of low, medium, and high-risk counties.
Methods: A 2010 national EMS database (NEMSIS) was joined to multiple sociodemographic databases. A negative binomial regression model identified predictors of prehospital naloxone use at the county level with the incidence rate ratio (IRR) as the measure of association. Risk profiles were produced for low, medium, and high-risk counties.
Results: Naloxone was administered in 52,014 of 6,746,334 scene calls (7.71 per 1000). The mean proportion of EMS calls by county where naloxone was administered was 5.83 per 1000, the median was 4.70 per 1000, and the range was 0–24.48 per 1000. County level risk factors were increasing proportion lacking health insurance (IRR 1.03: 95% confidence intervals (CI) 1.01–1.06), increasing median household income (IRR 1.08: 95% CI 1.05–1.10), increasing proportion receiving disability benefits (1.06: 95%CI 1.04–1.09), increasing infant deaths (IRR 1.03: 95% CI 1.02–1.05), census division (reference: New England; highest risk: South Atlantic IRR 2.44: 95% CI 1.82–3.27), increasing call proportion with EMS scene location at a home (IRR 1.10: 95% CI 1.05–1.15), increasing call proportion with EMS complaint of cardiac arrest (IRR 1.11: 95% CI 1.06–1.17), increasing call proportion where EMS transported the patient (IRR 1.12: 95% CI 1.07–1.17), increasing EMS use of antiemetics – a proxy for use of parenteral medications (IRR 1.08: 95% CI 1.06–1.10), longer EMS response time (IRR 1.06: 95% CI 1.03–1.10), and longer EMS scene time (IRR 1.04: 95% CI 1.02–1.06). Protective factors were proportion of EMS patients of black race (IRR 0.93: 95% CI 0.90–0.96), increasing median EMS patient age (IRR 0.98: 95% CI 0.97–0.99), and increasing time from EMS call to dispatch (IRR 0.91: 95% CI 0.88–0.94). The IRR for the lowest risk (1st percentile) county profile is 0.05 (95% CI: 0.02–0.13), median risk (50th percentile) is 7.78 (95% CI: 3.43–17.63), and highest risk (99th percentile) is 907.88 (95% CI: 304.20–2709.50).
Conclusion: There is wide county level variation in the use of naloxone. County level EMS and sociodemographic variables are important predictors of prehospital naloxone use.

53. Administration of expired methylene blue in patients with methemoglobinemia: A therapeutic dilemma

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Objective: To solve the problem of inadequate antidote stocking in Taiwan, the Taiwan National Poison Control Center established a nationwide antidote purchasing and stocking network in 2001. Life-saving antidotes that are rarely available, such as methylene blue, are then purchased collectively and distributed to selected acute care hospitals. Between December 2010 and October 2011, methylene blue was temporarily unavailable because the original manufacturer of methylene blue in the US suddenly discontinued the production of the drug. This left a period during which the administration of expired methylene blue in patients with methemoglobinemia became a therapeutic dilemma.
Case series: We reviewed the medical records of seven patients who were diagnosed as having methemoglobinemia during the period when only expired methylene blue was available, six patients (methemoglobin level ranging from 17.7 to 59.3%; median level 37%) received methylene blue therapy and all of them recovered within a short time. By contrast, a 70-year-old man who manifested coma and had a methemoglobin level of 62.7% after ingesting a feed additive did not receive methylene blue therapy. He gradually recovered after receiving endotracheal intubation with assisted ventilation and vitamin C injection but manifested worsening drowsiness and mental retardation in the next 3 weeks. Brain imaging studies eventually disclosed the presence of watershed infarct involving left centrum semiovale, corona radiata, and white matter of left anterior frontal and temporal-occipital area.
Conclusion: Methylene blue is an effective antidote for severe methemoglobinemia. However, the administration of expired methylene blue in patients with methemoglobinemia is of uncertain effectiveness and safety. Moreover, the use of an expired drug is against the law in Taiwan and the treating physicians are likely to be fined if the administered antidote is ineffective or even harmful. An efficient mechanism thus should be established to identify alternative supplier(s) for antidotes that will soon become expired. Careful examination of the quality of expired antidotes can also be conducted by the governmental regulatory agency to ensure that the drugs remain safe for use in case of medical emergencies. The poison control center can also provide expert opinion in the better management of acutely poisoned patients.

54. Symptomatic methemoglobinemia in a home hemodialysis patient and tolerance of methylene blue

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Objective: Methemoglobinemia is currently an extremely rare complication in home hemodialysis patients. However, contamination of the water circuit with an oxidizing agent is still possible. The tolerance of methylene blue is limited in anuric patients as the drug is also not eliminated by hemodialysis. We present a recent case complicated by significant hemolysis.
Case report: A 54-year-old anuric woman with end-stage renal disease treated by home hemodialysis was admitted to the emergency room (ER) for altered mental status, cyanosis, dyspnoea and nausea. Symptoms started a few hours before, at the end of a home hemodialysis session. There was no history of new drugs

prescription. Vital signs were: blood pressure 113/84 mmHg, heart rate 120 bpm, respiratory rate 40/min, SaO_2 94%. The diagnosis of methemoglobinemia (MetHb) was rapidly obtained, with an initial value of 20.9%. Severe hemolysis was simultaneously present, with Hb 4.7 g/dL. Methylene blue was administered at the dose of 1 mg/kg, with a second dose of 1 mg/kg after 1 h. Intubation was required for progressive worsening of neurological and respiratory status. The patient became hypotensive and norepinephrine infusion was started. Hemodialysis was also initiated. Due to persisting signs of hemolysis, partial exchange transfusion was considered. Extreme cyanosis persisted for several days, even when MetHb had dropped below 10%. Neurological and cardiocirculatory condition gradually improved and extubation was possible after 2 days. Hemoglobin electrophoresis was normal, with also no deficit in pyruvate kinase or G6PD; sulfhemoglobin was not found. Despite extensive toxicological investigations in serum but also in the fluids collected from different parts of the dialysis circuit, the offending agent could not be determined.

Conclusion: Acquired methemoglobinemia is now a rare complication in hemodialysis patients. With home dialysis, the risk exists that the circuit filled with tap water could be contaminated by an oxidizing agent, likely nitrate[1] or chloramine. Tolerance of methylene blue in anuric patients is usually poor at a dose greater than 1 mg/kg, with a possible worsening of neurological symptoms and hypotension.

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55. Seizures and sustained encephalopathy following an accidental 4-aminopyridine overdose

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Objective: 4-aminopyridine (4-AP) is a drug that enhances interneuronal and neuromuscular synaptic transmission. It can be used as adjunctive treatment for patients with multiple sclerosis (MS). Accidental or intentional overdose results in significant neurotoxicity.

Case report: A 58-year-old woman with secondary progressive MS was treated for more than 3 years with 4-AP (10 mg/bid) with an excellent tolerance. She was admitted to the emergency room (ER) with coma and convulsive status epilepticus. Symptoms started at home, a few minutes after the ingestion of one pill of 4-AP, with severe abdominal pain. The pill came from a new box of a pharmacy preparation that was supposed to contain 10 mg of 4-AP per pill. Less than 1 h after the ingestion, she developed rigidity, ocular revulsion, alteration of consciousness and finally generalized tonic-clonic seizures. No cardiac effects were observed; electrocardiogram was not modified. Intubation was required and the patient was administered three different anti-epileptic agents. No abnormal movements were observed. Electroencephalogram (EEG) recordings during the first 36 h showed abundant interictal epileptiform waves, predominant on the left hemisphere. Follow-up EEGs remained slowed and asymmetrical but confirmed the disappearance of epileptiform waves. The patient regained consciousness extremely slowly and remained seriously encephalopathic. Extubation was carried out on day 12. The patient did not recover completely. At 3-month follow-up, spastic paraparesis was more pronounced and increased cognitive impairment was documented, which slowly improved. 4-AP was not reintroduced. Laboratory analysis of the remaining pills showed that the capsules contained at least 80 mg 4-AP. Inquiry made in the pharmacy revealed that each pill was prepared with 100 mg 4-AP instead of 10 mg.

Conclusion: Error in the compounding pharmacy may lead to serious neurotoxicity in case of 4-AP overdose. Common manifestations include extrapyramidal movement abnormalities and seizures that can progress to status epilepticus. There is no specific treatment for 4-AP toxicity, except for seizure management. In contrast to the short elimination half-life of 4-AP, encephalopathy may be prolonged and some patients have presented long-term memory difficulties.[1]

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56. Adverse consequences of low-dose methotrexate medication errors

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Objective: To describe the consequences of medication errors involving low-dose oral methotrexate (MTX) prescribed on a weekly basis.

Methods: All cases involving an oral formulation of low-dose MTX and collected by the French network of poison control or pharmacovigilance centers from 2007 up to October 2013 were analysed. Cases were included if any of the following conditions were fulfilled: (1) intake of more than 2-fold the intended weekly dose, (2) a weekly cumulative dose higher than 30 mg, or (3) an error repeated for more than 7 consecutive days. A follow-up at least 4 days after the last MTX dose was also required in asymptomatic patients. The severity of symptoms was classified according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v4.03.

Results: 73 cases (54 females, median age: 76 years) were retained. The error occurred at home in 43 cases and in hospital or health care service in 28, and 16 resulted from a prescription error. Intake

of MTX daily instead of weekly was the most common (89%). The median duration of the error was 8 days (1–90 days). The median ingested dose was 7-fold (1.3–20) the intended dose and the median cumulative dose mistakenly received was 80 mg (20–300). The medication error was identified from symptoms suggestive of MTX toxicity in 67% of patients. Only 11 patients remained asymptomatic on follow-up. Among the 62 patients who developed complications attributable to MTX, 14 experienced minor symptoms and 47 had severe (≥ grade 3) complications, with oral mucositis and cytopenias as the most common. Overall, 9 patients died. As compared to patients with no or mild symptoms, those who experienced severe complications were significantly older (75.6 vs. 69.3 years), more likely to be treated already for a while (60% vs. 40%), to continue MTX for at least two additional days after the first suggestive symptoms of toxicity (26% vs. 8%) and to receive concomitant proton pump inhibitors (47% vs. 22%).

Conclusion: Even very small overdoses resulting from medication error with low-dose oral MTX can be dramatic. As a number occurred in hospital or a health care service, careful attention should be given when dispensing this medication.

57. A dietary supplement public health event

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Objective: OxyELITE Pro (USPlabs LLC; Dallas, TX, US) is a nationally marketed weightloss and bodybuilding supplement. In 2013, poison centers began reporting unexplained hepatic damage and deaths in chronic users. On 9 November 2013, as a result of investigations by US Centers for Disease Control and Prevention (CDC) and Food and Drug Administration (FDA) the manufacturer voluntarily recalled the product which contains alpha-yohimbine, *Bacopa monnieri* leaf, *Bauhinia purpurea* leaf and pod, caffeine, *Cirsium oligophyllum*, methylhexaneamine, and "proprietary blend". We describe these calls to one multi-state US poison center.

Case series: We queried the US National Poison Data System (NPDS) using the OxyELITE Pro product code (7259355) for our human exposures: 1 January 2012 to 15 November 2013. We stratified the data based on age, gender, chronicity, outcomes, and clinical effects. We collated the results using descriptive statistical measures.

Results: 20 and 25 exposures were identified in 2012 and 2013, respectively. One of our four states reported 58.5% of all exposures. 93% of exposures were single substance ingestions. 60% were female (in both years). The most frequent clinical effects are shown in Table 1. 68% and 55% of patients were ≤ 12 years of age in 2012 and 2013, respectively.

Table 1. Exposures to a dietary supplement.

	2012: n = 20	2013: n = 25*
Median age years (min-max)	2 (0.75–48)	3 (1–59)
Acute/chronic/unknown	25/0/0	14/4/2
Reason: suicide	6 (30%)	2 (8%)
Nausea and/or vomiting	6 (30%)	5 (20%)
Tachycardia	6 (30%)	3 (12%)
Hepatic abnormalities	0	4 (16%)
No or minor effect	20 (100%)	13 (52%)
Moderate	5 (25%)	3 (12%)
Major	0	2 (8%)
Death	0	1 (4%)

*2013 through 15 November.

Conclusion: Severity and number of chronic OxyELITE Pro cases increased from 2012 to 2013. Whereas no reports of hepatic dysfunction were reported in 2012, there were four cases in 2013. FDA chemical analysis revealed an unlabeled ingredient: aegeline which may be responsible for hepatic insufficiency and deaths. Poison centers can be an early warning system for detecting not only acute, but also chronic emerging public health events.

58. Persistent effects after camphor ingestion: A case report and review of the literature

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Objective: Camphor is found in many over-the-counter and traditional remedies. Severe ingestions may progress to seizures, apnea, and coma. The majority of case reports involving camphor ingestion demonstrate resolution of symptoms by 24–48 h, but physiologic derangement may persist.[1]

Case report: A 25-year-old Guatamalan woman with no past medical history presented to the emergency department (ED) for delirium 6 days after ingesting camphor for a rash. The patient's dose of camphor (117.53 mg/kg) was into the lethal range and she developed abdominal cramps, emesis, diarrhea, headache and vertigo. At home she remained mostly bedbound and slept throughout the day. Her husband described brief episodes of unarousability with generalized tremors that may have been seizures. The couple were illegal immigrants and were reluctant to seek medical attention. Initial vitals were heart rate 114, blood pressure 110/76, temperature 97.5°F, respiratory rate 23, and SpO_2 100%. She was oriented to person and place but not time. Initial treatment included 2 L 0.9% normal saline and 1 mg Ativan (lorazepam) intravenously. Her tachycardia resolved, but her delirium continued. She was admitted where she was monitored and underwent a normal computed tomography head and electroencephalography. The following day, her delirium resolved and the patient was discharged. However, she returned to the ED with persistent migraines 12 days later.

Conclusion: The exact mechanism behind camphor toxicity is not well understood. Short-term neurological effects may occur through noncompetitive inhibition of acetylcholine receptors.[2] Explanations for long-term toxic effects are unclear, but possible mechanisms include continued camphor release from fat stores or persistent axonal hyperexcitability after the initial insult.[3] Given the frequency of camphor poisoning in many parts of the world, particularly in certain underserved populations, it is vital to increase public awareness of camphor toxicity, understand the mechanism for toxicity, and develop targeted treatments.

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59. Vitamin D overdose in infants and newborns after medication error: Public health problem in Morocco

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Objective: To illustrate the problem of vitamin D overdose in Morocco we report a case of nephrocalcinosis in a 6-month old boy after administration of a high dose of vitamin D by his mother
Case report: A previously healthy 6-month-old boy was admitted to the emergency department with acute vomiting and irritability. Physical examination revealed mild dehydration, drowsiness, axial hypotonia of axial and limb muscles, lethargy and tachycardia (130 beats per minute). The serum levels of urea, creatinine, sodium, potassium, uric acid were normal, but serum calcium level was 130 mg/mL. Abdominal ultrasound revealed bilateral medullary nephrocalcinosis. The mother revealed that her child received a dose of vitamin D at the hospital and thereafter she had given him several ampoules of vitamin D each day. She had bought the ampoules from the pharmacy without a prescription to increase the effectiveness of the administered dose in the hospital. The infant was admitted to the intensive care unit. Treatment consisting of hydration with parenteral fluids, furosemide (20 mg/kg) and corticosteroid (2 mg/kg/day) was started. The level of serum calcium decreased and returned to normal limits in 9 days.
Conclusion: Many actions including a parent education program and informing health care professionals about the risks related to vitamin D overdoses have been taken by the Pharmacovigilance Centre of Morocco and Pediatrics to reduce the incidence of vitamin D overdose. In addition, the dose of vitamin D given by the national program for preventing rickets will be reduced to 200,000 IU.

60. AV block II in a toddler after accidental ingestion of a single tablet of fingolimod for multiple sclerosis

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Objective: Fingolimod is a new oral drug for treatment of multiple sclerosis in adults.[1] It is known that fingolimod therapy commonly carries adverse reactions such as a negative chronotropic effect and an increased atrioventricular conduction time in adolescents and adults.[2] However, the drug is not used in children and reports describing the consequences of fingolimod in overdose are totally lacking.
Case report: A healthy 4-year-old boy ingested one 0.5 mg Gilenya tablet (fingolimod) i.e., the daily dose for an adult. The pharmaceutical was prescribed for his mother who immediately discovered the accident. She called the poison center who arranged urgent transport to hospital. The patient received charcoal in the ambulance 45 min post-ingestion. On arrival at the emergency department 90 min post-ingestion the boy was unaffected. His heart rate was 87 bpm and blood pressure 108/70 mmHg. The electrocardiogram (ECG), however, displayed AV block I with a PQ-time of 196 ms. The patient was placed on observation including continuous cardiac monitoring. During the period between 2 and 10 h post-ingestion, cardiac monitoring displayed bradycardia in relation to age, 58–78/minute, and AV block I alternating with AV block II with Wenckebach phenomenon. The blood pressure measurements during the same period showed hypotension down to 77/34 mmHg. The patient was discharged in a good condition after 24 h. At follow-up 2 days later the ECG displayed normal sinus rhythm with a PQ-time of 164 ms and normal liver function tests.
Discussion: Fingolimod is an immunomodulating agent developed for preventing rejection of renal transplant. Its ability to keep lymphocytes in the lymph nodes has been found useful in the treatment of multiple sclerosis.
Conclusion: We would like to emphasize the risks involved with this relatively new pharmaceutical, especially among children, as one single tablet apparently is enough to cause serious reactions.

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61. Asymptomatic rhabdomyolysis after pyridoxine treatment of an isoniazid intoxication

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Objective: To report a case of asymptomatic rhabdomyolysis.
Case report: A 22-year-old man of Asian origin deliberately ingested 75 × 100 mg tablets isoniazid. Half an hour later he developed a cerebral seizure. However, he was fully awake (Glasgow Coma Scale (GCS) 15) 30 min after the ambulance arrived. The consulted emergency physician documented somnolence (GCS 8) and another seizure. The patient was sedated with midazolam and fentanyl, orally intubated and mechanically ventilated. At admission 90 min after ingestion he was cardiorespiratorily stable. However he had a marked metabolic acidosis (pH 6.98), an increased lactate (at admission 20 mmol/L, which declined to 0.7 mmol/L after 7 h) and an increased serum-creatinine (1.2 mmol/L at admission). Creatine kinase (CK) rose within 3 h from 581 U/L to 1135 U/L. Electrocardiogram (ECG) showed multiple ventricular extrasystoles. The patient received 40 mg diazepam and 5 g pyridoxine intravenously within 30 min. The level of isoniazid fell from 16 μg/mL 2 h after ingestion to 13.5 μg/mL 20 min later. The

acidosis resolved and the patient regained sinus rhythm. After stopping sedation the patient could be extubated 18 h after ingestion. The further course was uneventful and the patient was transferred to a psychiatric ward 4 days after ingestion. Meanwhile, the patient had a remarkable course of rhabdomyolysis, which was clinically inapparent. At admission (t = 2 h) his CK was 581 U/L and increased to 1135 U/L (t = 5 h). At day 5 it rose to 29,000 U/L. The patient was therefore transferred back to the medical ward. Here, the CK returned to normal values under symptomatic observation. The patient never exhibited clinical symptoms of rhabdomyolysis nor renal failure. In the literature rhabdomyolysis after isoniazid intoxication treated with pyridoxine is rarely reported, with an incidence of 3%. In all cases from the literature as well as ours rhabdomyolysis was restricted to pathological CK-values only. Patients never developed further complications such as respiratory or renal failure. The pathomechanism of rhabdomyolysis in the course of isoniazid intoxication treated with pyridoxine is not known.
Conclusion: Rhabdomyolysis after isoniazid intoxication and pyridoxine treatment is an infrequent, but known complication. Specific therapy is not necessary. Repeated evaluation of renal function along with rehydration seems sufficient.

62. A case report of exogenous human chorionic gonadotropin use leading to laparoscopy to exclude ectopic pregnancy

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Objective: Oral exogenous human chorionic gonadotropin (HCG) products are readily sold online and over-the-counter as diet agents, despite lack of evidence to support weight-loss claims. We report a unique case of a patient on an "HCG diet" who required laparoscopic surgery to exclude ectopic pregnancy.
Case report: A previously healthy 30-year-old woman presented to the emergency department (ED) with sudden onset lower abdominal pain and syncope. Six days prior she started an "HCG diet", a calorie restricting diet (500 Kcal/day) coupled with 12 sublingual drops (200 IU) HCG TID.[1] The product was purchased online with active ingredients labeled as HCG, L-arginine, acetyl L-carnitine, and L-omithine. Vital signs include blood pressure, 115/56 mmHg; heart rate, 117/min; respiratory rate, 18/min; temperature, 98.2°F. Her last menstrual period was 6 weeks prior to presentation. Serum quantitative HCG was 218.9 mIU/mL and pelvic examination revealed poorly localized bilateral adnexal tenderness. Emergent transvaginal ultrasound (TVUS) to exclude ectopic pregnancy revealed a moderate amount of free fluid in the right adnexal region, a 12×2.9 cm heterogenous collection posterior to the uterus, an enlarged left ovary with heterogenous echotexture, and no intrauterine gestation. Ruptured ectopic pregnancy could not be excluded and she was admitted for observation. On day two, HCG was 352.5 mIU/mL, pain was improving, and she was discharged. Despite plan for 48-h follow-up, the patient presented 6 days later with persistent abdominal pain and quantitative HCG 75.6 mIU/mL. Emergent laparoscopy was performed to exclude ectopic pregnancy and revealed a left-sided hemorrhagic cyst.
Conclusion: Exogenous HCG supplementation in this case led to an invasive procedure to rule out ectopic pregnancy. This case displays the dangers of HCG supplementation in premenopausal women. Given that TVUS identification of ectopic pregnancy is often difficult, physicians rely on changes in serial serum HCG concentrations to exclude ectopic pregnancy. Currently there is no readily available laboratory assay to distinguish between exogenous and endogenous HCG. Exogenous HCG use may complicate interpretation of serum HCG levels and lead to unnecessary invasive procedures.

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63. Metformin induced leukemoid reaction

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Objective: A leukemoid reaction describes a leukocytosis that is a physiological response often to stress or infection as opposed to a primary blood malignancy. Several medications have been described as possibly causing a leukemoid reaction. Our objective is to, to the best of the authors' knowledge, describe the first metformin induced leukemoid reaction
Case report: A 19-year-old male presented to the hospital 2 h after ingesting 240 tablets of metformin 500 mg. The patient was awake and alert, but had violent retching without vomiting. Vital signs at that time: blood pressure 120/71 mmHg; pulse 112 beats/minute; oxygen saturation 97% on room air, afebrile. Basic metabolic panel at that time revealed a CO_2 of 14 mmol/L, a lactic acid of 7.2 mmol/L, a pH of 7.38, and a white blood cell count of 13.4 K/μL with no bands. All other labs were non actionable, including ethanol, acetaminophen, and salicylate. Repeat laboratories done 8 h after presentation and after 4 h of dialysis revealed a CO_2 of 10 mmol/L, a lactic acid of 30.6 mmol/L, a pH of 7.08, and a white blood cell count of 43.7 K/μL with 6% bands. Eosinophils were within the normal range throughout. Approximately 16 h post-ingestion, the patient had a white blood cell count of 62.6 K/μL with 23% bands. The patient continued to deteriorate, and despite an additional hemodialysis session and multiple vasopressors, died shortly thereafter.
Conclusion: Massive overdose of metformin can lead to a leukemoid reaction, resulting in markedly elevated white blood cells and bandemia. There was no indication that eosinophils predominated which helps eliminate the probability of a hypersensitivity response.

64. Post-injection delirium/sedation syndrome after olanzapine pamoate intramuscular injection confirmed by serum olanzapine concentrations

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Objective: This is a report of a very rare case of a serious adverse event termed "post-injection delirium sedation syndrome" (PDSS) due to intramuscular injection of olanzapine pamoate, with symptoms similar to those of serious acute oral olanzapine intoxication, confirmed by olanzapine concentrations in serum using liquid chromatography-tandem mass spectrometry (LC-MS-MS).
Case report: A 60-year-old schizophrenic female, underweight (body mass index (BMI) 18.2 kg/m^2), was admitted to the Toxicology Department with suspicion of olanzapine intoxication. The patient lost consciousness 10 min after the fourth intramuscular injection of 405 mg olanzapine pamoate, which was administered every 4 weeks. She was unconscious, periodically agitated, with slight rigidity in extremities and asymmetric abnormal flexion to painful stimuli, bilateral miosis, increased body temperature (38.2°C), tachycardia (112–130/min) and blood pressure 140/75 mmHg. Due to upper airway obstruction intubation was performed, but mechanical ventilation was not necessary. After 24 h symptomatic therapy the patient was extubated. She remained moderately somnolent, confused, with slurred speech, unable to carry out simple commands. Forty-eight hours after the injection the patient was fully conscious but significantly weakened. She was discharged from the hospital after 5 days. Blood laboratory tests were on the normal ranges. Quantitative determination of olanzapine in serum was performed by LC-MS-MS. At 5, 14, 24 and 48 h after injection drug levels were 698, 530, 455 and 271 ng/mL, respectively (recommended therapeutic concentration 20–80 ng/mL).
Conclusion: PDSS is a rare (0.07% of injections) but serious adverse events of therapy with olanzapine pamoate in which very high olanzapine levels that can exceed 600 ng/mL, as here, have been observed. Because of a wide interindividual variability in olanzapine pharmacokinetics and unidentified risk factors, therapeutic drug monitoring may be a valuable tool for both safety and effectiveness of therapy. The lower BMI and greater age of the patient could have increased the risk of PDSS in our case. Reporting of all cases of PDSS with a careful description of symptoms and assessment of drug concentrations may contribute to increasing the knowledge about this rare syndrome.

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65. Toxic epidermal necrolysis associated with lomefloxacin: Case report and molecular typing studies

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Objective: Toxic epidermal necrolysis (TEN) is a severe cutaneous adverse reaction (SCAR) that may occur in patients treated with several drugs. Only mild cutaneous reactions such as photosensitivity have been described related to lomefloxacin hydrochloride.[1] We describe a case of lomefloxacin-related TEN in which a key role of the human leukocyte antigen (HLA) has been identified.
Case report: A 30-year-old Caucasian woman, with negative history for allergy to drugs, was admitted to the emergency department for chills, dysuria, strangury, and fever (37.5°C). A urinary tract infection was suspected and lomefloxacin (400 mg/day) was prescribed. A few hours after taking the first lomefloxacin tablet, the patient noticed the appearance of vesicular lesions in the genital area. Rubella was suspected and acyclovir (500 mg) was prescribed, with associated intravenous methylprednisolone (40 mg) and paracetamol (1000 mg) due to persisting fever. The patient presented a fast onset TEN occurring 24 h after the first lomefloxacin tablet administration, with skin blisters and disepithelization involving 90% of total body surface area within 48 h. Burn Unit admittance was required and specific treatment based on corticosteroids and human intravenous immunoglobulins was started. Progressive improvement led to complete recovery in 3 months. A 14-month follow-up after the TEN onset showed complete neurological recovery, with no residual motor or sensory impairment, and a reduction in the extension and pigmentation intensity of the cutaneous changes. The patient still presented xerostomia, mainly involving conjunctiva and vaginal mucosa and skin discolorations were still under dermatological treatment. Molecular studies showed an uncommon immunogenetic profile characterized by excess of HLA ligands and killer-cell immunoglobulin-like receptors inhibitory pairs conjugated with an HLA-DR,DQ haplotype prone to autoimmunity.
Conclusion: Early clinical recognition and early patient referral to a specialized care facility is of crucial importance in life-threatening SCAR. A combined KIR and HLA involvement in drug-induced SCAR may be hypothesized in any severe case, and play a critical role in difluoroquinolone drug therapy assessment.

Reference

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66. Encephalopathy due to prolonged misuse of ivermectin (Stromectol R) after scabies infection

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Objective: To describe a case of chronic ivermectin overdose resulting in encephalopathy.
Case report: For the treatment of scabies, a 41-year-old woman was prescribed one single dose of four 3 mg ivermectin tablets. Because of persistent pruritus on hands and feet, she decided to prolong the

treatment and repeated the intake of four tablets every week during 6 months. Two weeks before admission, she increased the dosage to four tablets a day. She was brought to the emergency department (ED) by her husband because of vertigo, somnolence, speech problems, and abnormal movements of 4 days duration. Her husband said that she was confused and disoriented in time. On examination, she was effectively confused and apathetic, with a slow and dysarthric speech. She presented myoclonia of the hands. The electroencephalogram (EEG) showed generalized slowing and depressed reactivity. The computed tomography (CT) scan and the magnetic resonance imaging (MRI) were within normal limits. The dermatologist confirmed the absence of scabies and the presence of scratch lesions on hands and feet. The patient did not take ivermectin on the day of admission. She was advised to immediately stop ivermectin and she was treated with cetirizine against pruritus. Two days after stopping ivermectin, the neurological symptoms improved. The victim could leave the hospital 3 days after the last ivermectin intake.
Conclusion: Persistent pruritus after scabies can lead patients to unduly prolong their treatment. With ivermectin, this misuse can result in encephalopathy. After stopping the medication, symptoms improved within a few days, which corresponds to the ivermectin half-life of 18 h. We did not find in the literature any similar case of prolonged ivermectin overdose.

67. Chlorine dioxide from a dietary supplement causing hemolytic anemia

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Objective: Miracle Mineral Solution (MMS) has been marketed as an alternative treatment for HIV, hepatitis, common colds, acne, cancer, and other conditions. However, MMS, a 28% sodium chlorite solution that produces chlorine dioxide when mixed with its acidic "activator", carries serious health risks. Despite warnings from multiple national agencies, including the Food and Drug Administration (FDA) in 2010, many hopeful patients still use this product. We report a unique case of severe hemolytic anemia after use of MMS.
Case report: A 75-year-old man with a history of stage IV prostate cancer on monthly leuprolide presented with worsening fatigue, shortness of breath, and lightheadedness, 7 days after ingesting MMS that he purchased over the Internet. The patient stated that he used 100 drops (~5 mL) of the MMS with the activator, more than the recommended 1–3 drops, with hopes of increased efficacy. Four hours later, he developed abdominal pain and vomiting. These symptoms slowly abated over the next 2 days, but he began to develop worsening fatigue. Systemic examination was unremarkable. Investigations revealed a hemoglobin concentration of 5.5 mg/dL (from a baseline hemoglobin of 10.5 mg/dL), lactate dehydrogenase of 1491 U/L, and haptoglobin < 10 mg/dL. The patient was supported with blood transfusions and recovered fully. He was advised to discontinue the use of this supplement and the adverse event was reported to the FDA.
Conclusion: Chlorine dioxide has been linked to acute hemolysis, methemoglobinemia, and kidney failure due to its oxidant properties. MMS is not approved in the US for the treatment of any disease and according to the FDA, "consumers who have MMS should stop using it immediately and throw it away." To date, there have been no other case reports of MMS causing severe, symptomatic hemolysis. It is thus important to note that patients who consume MMS can manifest severe, symptomatic hemolysis.

68. Methemoglobinemia in long term dapsone treatment

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Objective: Methemoglobinemia is a hematological disorder clinically characterized by the bluish color of the extremities, general manifestations and even death at high blood levels of methemoglobin (MetHb). One of the most commonly used sulfones in cutaneous problems is dapsone. Dapsone is metabolized by the liver and N-hydroxylation results in its metabolite aminohydroxylaminodiphenylsulfone which can induce methemoglobinemia, hemolytic anemia and Heinz body formation. We present a case of dapsone induced methemoglobinemia.
Case report: A 43-year-old woman, with systemic vasculitis and cutaneous lesions, treated with dapsone 100 mg/day for 4 months was admitted after a fainting episode and diarrhea. On admission we found a weak and anxious patient with cyanosis of the extremities and livedo reticularis of the legs, intense cephalea, dizziness, and nausea; she was tachypneic, with non-invasive blood pressure (NBP) = 100/50 mmHg, tachycardia 125 b/min, and pulse oximetry 72%. The investigations showed anemia (Hb 10.9 g/dL, Ht 31.4%), high blood levels of MetHb (23.2%), low levels of oxygen blood pressure and high levels of blood CO_2 ($pO_2 = 29.8$ mmHg and $pCO_2 = 46.9$ mmHg), total bilirubin = 1.9 mg/dL with indirect bilirubin higher. The first therapeutic action was stopping the agent that caused the methemoglobinemia and starting oxygen therapy. Methylene blue 1 mg/kg was administered intravenously, along with ascorbic acid 1 g and volume repletion. The patient's symptoms disappeared and the level of MetHb after 2 h was 4.4%. The patient was discharged after 3 days, with MetHb = 1.2%, Hb = 11.7 g/dL and normal bilirubin level. She was advised not to use dapsone for her cutaneous problems.
Conclusion: Methemoglobinemia is a rare disease, with complete recovery in mild forms. The most common cause of acquired methemoglobinemia is drugs. In our case methemoglobinemia was secondary to a usual dose of dapsone. Early diagnosis of methemoglobinemia and discontinuation of dapsone administration with the establishment of specific therapy allowed the remission of methemoglobinemia manifestations without complications.

69. Medication errors in the first 6 months of life

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Objective: Medication errors (ME) represent a threat to health both at home and in the hospital setting. Newborns and infants constitute a group of patients at high risk of developing severe clinical effects, because of their low weight and physiological characteristics. There is, anyway, a lack of data concerning drug toxicity in newborns and infants. The objective is to evaluate ME in the first 6 months of life which come to the attention of Pavia Poison Center, and to identify major risks and to focus on corrective actions.
Methods: A 6-year retrospective study (2007–2012) was performed; all the cases of ME in infants younger than 6 months referred to our poison control center (PCC) were evaluated. Data about patients and intoxication circumstances were collected and analyzed.
Results: 561 cases were analyzed. One hundred and fifty out of 561 patients (26.8%) were less than 1-month old. Fifty-five per cent of errors occurred between 4 and 12 pm. Most of the events (89.8%) consisted of administration errors by relatives, whereas 10.2% were iatrogenic. In 52.9% of cases (257/561) a drug different from the prescribed one was given; in 39.5% (222/561) the administered dose was wrong; in 23/561 (4%) the mistake was regarding the administration route. Preparation errors of drugs occurred in 15 cases, whereas expired drugs were given in 4 cases. The drugs most involved were vitamins (n = 70), gastrointestinal drugs (n = 69), paracetamol (n = 67), methylergometrine (n = 63), antibiotics (n = 55). Symptoms occurred in 104/561 patients (18.5%), and were mainly neurological (agitation in 18.1%, drowsiness in 36.1%) and gastrointestinal (vomiting in 16.2%, diarrhea in 9.5%, abdominal colic in 6.7%). 12.5% of patients showed tachycardia and 67% had unexplained crying. Among symptomatic patients, 71 presented with mild symptoms (68.26% PSS1), 31 moderate (29.8% PSS2) and 2 severe (1.92% PSS3). No lethal cases were observed. The drug categories that most often caused symptoms were antihistamines (15/43; 34.9%); neuropsychiatric/opioid drugs (12/34; 35.3%); antiasthmatics (10/24; 41.7%).
Conclusion: The ME were mainly due to parents' inexperience, especially when involving new parents, or when similar-named drugs, and large number of medicines were given to newborns and infants. Sometimes, prescriptions are difficult to interpret, as well as drug dosing indications. Moreover, leaflets may contain terms difficult to understand by non-native Italian speakers.

70. Non-ST-segment-elevation myocardial infarction after phenylephrine misdosing

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Objective: To report a case of non-ST-segment-elevation myocardial infarction (NSTEMI).
Case report: A 68-year-old male with medical history of hypertension and deep venous thrombosis presented from the Post-Operative Care Unit (PACU) to the emergency department complaining of chest pain. During his nasal surgery, the patient inadvertently received 1000 μg of intravenous (IV) phenylephrine, as opposed to the intended dose of 100 μg. The dosing error was a result of inconsistent medication preparation. As a result, the patient's blood pressure quickly spiked to a blood pressure of 240/115. His heart rate briefly dropped to 40 beats per minute (bpm) and then accelerated to 120 bpm. During this case time, the cardiac monitor showed roughly 60 s of ST depression. The anesthesiologist quickly realized the error and controlled the patient's blood pressure with propofol. The patient's abnormal vital signs resolved in less than 10 min. The patient's first troponin was elevated to 2.1 μg/L (abnormally high above 0.03 μg/L). Two hours later, his troponin had increased slightly to 2.2 μg/L and his chest pain persisted. At this point, he was admitted to the cardiology service. Heparin was not used as the patient was experiencing post-operative epistaxis. Overnight, his troponin peaked at 2.54 μg/L, but by morning had decreased to 1.18 μg/L. A resting transthoracic echocardiogram showed no evidence of acute cardiac injury.
Conclusion: This case report describes a patient who experienced a non-ST-segment-elevation myocardial infarction (NSTEMI) secondary to extreme hypertension after an accidental overdose of phenylephrine. As many physicians work at multiple practice locations, we present this case in order to emphasize both the importance of consistent medication labeling and delivery practice. Also, as many patients use alpha agonist medications of varying delivery method and preparation, we emphasize the importance of taking a thorough medication history that includes over the counter preparations, daily medications, and recent surgical medications as the side effects caused by alpha agonists can be extreme and are not entirely dose-dependent.

71. Topiramate-associated heat stroke resulting in disseminated intravascular coagulation

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Objective: Describe a case of topiramate associated heat stroke resulting in disseminated intravascular coagulation.
Case report: A 38-year-old man was found unresponsive next to his lawn mower after mowing the lawn. The maximum ambient temperature that day was 28.9°C (84°F). He was transported to the emergency department and found to have the following vital signs: temperature 42.1°C (rectal), blood pressure 110/40 mmHg, pulse 160 beats/min, and oxygen saturation of 89% on room air. He had no signs of rigidity, hyperreflexia, or trauma. He was intubated and hyperthermia was managed with a cooling blanket and multiple liters of cooled saline intravenously. The patient's prescription medications included topiramate and carbamazepine and he had recently been started on risperidone. Over the next 24 h, the patient developed multi-organ dysfunction including disseminated intravascular coagulation, acute kidney injury, hepatic injury, and hypotension. This was further complicated by ischemic gastritis, upper gastrointestinal bleeding, and gastric perforation requiring complete gastrectomy. After a prolonged hospitalization, he was discharged to a nursing home. Cultures of blood, urine, cerebrospinal fluid (CSF), and stool were unrevealing. Electroencephalography demonstrated no evidence of seizure activity. A urine gas-chromatography/mass spectrometry (GC/MS) qualitative drug screen detected only topiramate. Computed tomography (CT) imaging of head, neck, chest, and abdomen were unremarkable. The patient's co-workers reported no alteration of his mental status on the day of his presentation to the hospital.

Conclusion: In agreement with other case reports, therapeutic use of topiramate may predispose individuals to exercise-induced heat stroke and permanent morbidity in adults.

72. Reversible cardiomyopathy secondary to citalopram and methadone toxicity

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Objective: To describe a case of reversible cardiomyopathy secondary to citalopram and methadone toxicity.
Case report: A 19-year-old man with a history of depression prescribed citalopram was found unresponsive at home. Paramedics administered naloxone which caused vomiting and seizure-like movements. He had minimal improvement in level of consciousness and was therefore endotracheally intubated on scene. The patient's vital signs on arrival to the emergency department (ED) were: blood pressure 130/82 mmHg, heart rate 89 bpm, respiratory rate 14 rpm, temperature 29.3°C rectally, O_2 saturation 100% on 80% FiO_2. Electrocardiograph (EKG) demonstrated atrial fibrillation at 81 bpm, with QRS and QTc intervals of 168 and 592 ms, respectively. Serum troponin I measured 0.690 ng/mL (0.0–0.045). Arterial blood gas (ABG) analysis measured: pH 7.04, PaO_2 94, $PaCO_2$ 81, and bicarbonate 26 mmol/L. Serum salicylate, acetaminophen, and ethanol levels were undetectable. The patient was then transported to a tertiary care center. During transport, he became hypotensive and was administered intravenous (IV) norepinephrine (NE). On arrival to the tertiary center intensive care unit (ICU), the patient's physical exam was remarkable for hyperreflexia and clonus. Following a nadir of his blood pressure at 75/42 mmHg, the NE infusion rate was increased and a dopamine infusion was initiated. Following these measures, he spontaneously converted to normal sinus rhythm. Hypothermia was corrected rapidly with active external rewarming. Serum lactate and creatine phosphokinase (CPK) peaked at 5.0 mmol/L (0.5–1.6) and 5807 IU/L (0–200), respectively. A transthoracic echocardiogram (TTE) performed several hours after arrival showed: a non-dilated left ventricle with an ejection fraction of 10–15%, akinesis of the inferior septum and mid and distal inferior wall, and hypokinesis of the remaining walls. Based upon the appearance of cardiogenic shock, dobutamine was then administered. Over the course of 24 h, vasopressors were successfully discontinued. The respiratory acidosis and hyperlactemia corrected. Serum troponin I peaked at 2.89 ng/mL. Repeat TTE on hospital day four showed complete normalization of heart function. Comprehensive urine drug screen detected large peaks of citalopram and methadone. He was discharged without sequelae to an inpatient psychiatric hospital on hospital day 6.
Conclusion: Acute citalopram and methadone toxicity can lead to a reversible cardiomyopathy. Aggressive supportive care and vasopressor therapy are warranted to allow for clinical resolution.

73. Medication incidents in primary care medicine: Prospective observational pilot study with case-control analysis

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Objective: Medication incidents (MIs) can lead to increased and prolonged hospitalization, adverse health outcomes, additional use of resources, and increased healthcare costs. Although most research has been conducted in the inpatient setting, evidence indicates that adverse drug events pose a serious threat also to patients in primary care. The aims of this pilot study were to obtain preliminary data on frequency, type, severity, and predisposing factors for MIs in outpatients and to investigate the feasibility of a national systematic prospective registration of MIs in primary care.
Methods: Prospective registration of MIs among 18 Swiss general practitioners (GPs) and practicing pediatricians located throughout the country between July and September 2013. To identify predisposing factors, for each case we collected information from a control patient, matched on age and gender. Medians and interquartile ranges (IQR) were calculated and differences between cases and controls were analyzed by chi-square test.
Results: During the study, the median number of patient contacts per physician was 686 (IQR 320); GPs had 93 (37) contacts per week, and pediatricians 87 (45). Overall, 50 MIs were reported by GPs, and 1 by pediatricians. The incident rate per GP was 0.4 (median, IQR 0.4) per week, and 4 (5) per 1000 contacts. Males were involved in 26 cases (51%), and the median age was 67 (23) years. The two most common types of MIs were adverse drug reactions (18 cases, 35%) and supratherapeutic doses (10, 20%). Magnitude of the overdose was limited to inadvertent doubling of the therapeutic dose in most cases, and the drug classes most frequently involved were antidiabetics, corticosteroids, and anticoagulants (2 cases each). Overdose patients were asymptomatic or had minor consequences, except for 1 case of severe hypoglycaemia due to insulin, and no patient required hospitalization. Case-control analysis did not reveal any obvious predisposing factors for MIs, although there was a tendency that cases were more likely to be on psychotropic drugs than controls (41% vs. 22%, $p = 0.14$).
Conclusion: Minor overdoses seem to be a common type of MI in primary care. The systematic prospective registration of MIs appears feasible in our country and may contribute to postmarketing drug safety surveillance.

74. Benzyl benzoate burns bad: 339 poison center adverse reaction reports and counting

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Objective: Benzyl benzoate is a topical treatment for scabies and body lice. The two Australian formulations, Ascabiol and Benzemul are both 25% concentration, dilution is recommended prior to use for children. The limited clinical trial data on its use (10–25% concentration) suggests similar effectiveness to permethrin; dermatological adverse reactions were reported but were classed as minor with incidence of 0–38%.[1] The aim of this study was to describe the nature and frequency of adverse drug reactions (ADRs) to topical benzyl benzoate reported to the largest Australian poisons center.
Methods: A retrospective review of calls made to New South Wales Poisons Information Centre (NSWPIC) during 1 January 2004–30 September 2012 involving adverse reactions from therapeutic use of benzyl benzoate.
Results: 339 cases were reported, with the annual incidence doubling to 2011. Two hundred and thirteen reports involved children (< 18 years), 89 were under 5 years. 64.5% involved Ascabiol and 35.5% Benzemul. Forty-four presented to or were referred to a medical practitioner or hospital, with an additional 22 ambulance call-outs. Two hundred and forty-two people reported severe burning/stinging sensation, 65 erythema, and 16 rashes. The most commonly affected areas were the genitals, face, and neck region. Topical permethrin has a significantly larger market share in Australia, however only 21 ADRs were reported to NSWPIC in the same time period. Since 2000, the Australian Therapeutic Goods Administration and Adverse Medicine Events Line only had 5 ADRs reported from benzyl benzoate and 46 cases during 1975–1999.
Conclusion: Use of benzyl benzoate is a cause of significant pain and distress. Adequate counselling for consumers on appropriate first-line therapy (permethrin as per Australian Therapeutic Guidelines), correct usage and possible adverse effects is vital. PICs are an underutilized source of ADR reporting.

Reference

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75. Toxicokinetics of intravenous paracetamol overdose in a 13 kg girl

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Objective: Use of intravenous (IV) paracetamol (APAP) has increased in the United States since its Food and Drug Administration (FDA) approval in 2010. Reports of medication errors are rare, outcomes are poorly documented, and toxicokinetic data in the literature is lacking. We report a case of IV APAP overdose with sequential APAP concentrations.
Case report: A 2-year-old, 13 kg girl undergoing elective tonsillectomy received cefazolin (1000 mg IV) and APAP (1000 mg IV) (77 mg/kg for both) in the operating room around the start of surgery. The intended doses were APAP 195 mg (15 mg/kg) and cefazolin 325 mg (25 mg/kg). The error was noted upon emergence from anesthesia. She was extubated and transferred to the Pediatric Intensive Care Unit, where her initial vital signs were: blood pressure, 105/35 mmHg; heart rate, 104/min. Her postoperative course was unremarkable. 2.4 h post administration, her serum APAP concentration was 417 μmol/L (63 μg/mL); AST, 36 U/L; ALT, 7 U/L. Serum APAP concentrations were 291 μmol/L (44 μg/mL) and 238 μmol/L (36 μg/mL) at 4.3 h and 5 h post-administration respectively. Her AST and ALT did not rise after 28.5 h and the patient remained asymptomatic. N-acetylcysteine was not administered due to the theoretical low risk for hepatotoxicity of the exposure weighed against the risk of administering N-acetylcysteine. With only three serum APAP concentrations taken in close proximity to each other, it is difficult to clearly determine whether first-order or zero-order elimination kinetics predominate. Assuming first-order elimination, a linear relationship was noted between the natural logarithm of the serum APAP concentrations over time ($R^2 = 0.9903$) and the calculated half-life was 3.30 h. Prior reports that suggest the APAP half-life in children is 1–3.5 h are consistent with this finding. Assuming zero-order elimination kinetics a linear relationship was also noted ($R^2 = 0.9991$) and the rate of elimination was 68 μmol/L/h (10.3 μg/mL/h).
Conclusion: We report a patient with an iatrogenic IV APAP overdose of 77 mg/kg not treated with N-acetylcysteine who did not develop hepatotoxicity. Given the number and temporal relationship of serum samples, we are unable to find a significant difference between first- and zero-order models of elimination kinetics.

76. Neonatal medication errors reported to a poison control center

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Objective: Medication errors in neonates are rarely reported to poison centers, but are potentially serious. We aimed to characterize neonatal exposures with regard to high-risk medications and medication classes and the causes of error.
Methods: This is a retrospective case-series of medication errors reported to a regional poison center in children less than 30-days old between 1 January 2000 and 12 November 2013. Data extracted included the year of exposure, age (days), exposure, type of error (wrong dose, medication, patient, dosing interval, or formulation, ten-fold (10x) exposure, pump malfunction or double administration) and sequelae. Cases were excluded if the exposure was uncertain or if the sequelae were associated with an adverse effect of an appropriately ordered and administered medication.
Results: 38 cases were located and 7 were excluded. Between 2000 and 2013 there were 1–6 exposures per year, though there was no trend. The median age was 6 days (range 1–27). The most frequent medication class associated with an error was antimicrobials (11/31)

followed by antiretrovirals (4/31). Specific medications with the largest number of errors were vancomycin (4), gentamycin (3), paracetamol (3), and zidovudine (3). Dosing errors predominated with 21/31 cases given the wrong dose including 7/31 that were 10x exposures. Four were given the wrong medication: two were given methylergonovine and one was given Rho(D) Immune Globulin that were meant for the mother. One was given pentobarbital when phenobarbital was ordered. The assessment of adverse events is complicated by the patients' underlying conditions. Seizures were associated with one given methylergonovine, one given a 10x dose of carbamazepine, and one given the wrong formulation of amphotericin. Hypoxia and hypotension developed after a pump malfunction and intravenous administration of fentanyl. Cardiac arrest and the subsequent use of vasopressors occurred in a child given two times the intended dose of flecainide.
Conclusion: While rare, reported neonatal medication errors are associated with significant consequences. Neonatal dosing of medications is the greatest factor in the commitment of errors. Incorrect medication administration and the administration of medication to the child that was intended for the mother were associated with significant adverse effects.

77. Enquiries from nursing homes – increasing problems?

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Objective: Since 1999 the regional poisons center (PC) observed a continually increasing number of enquiries from nursing homes for handicapped and elderly people. This study is meant to show the relevance in the everyday work of the PC and intends to describe underlying reasons.
Methods: Retrospective analysis of PC data from 1999 to 2012: human exposures in nursing homes; further analysis including epidemiology and clinical presentation.
Results: Total number of enquiries from nursing homes: 2157. Increasing trend from 1999 to 2012: 48–313 cases (+ 652%) respectively 2.4% to 9.9% of all PC-cases (+ 412%). Type of caller: medical staff e.g., physician, ambulance (n = 735; 34%) increased from 26 to 89 calls/year (+ 324%), laymen and nursing staff (n = 1422; 66%) increased from 22 to 224 calls/year (+ 1018%). Reason: accidental (n = 814; 84%) continuously increased from 34 to 296 calls/year (+ 871%), cases with all other reasons (n = 343; 16%) remained constantly less than 44 calls/year. Cases with an accidental exposure not involving medication (n = 684; 32%) increased from 22 to 85 calls per year (+ 386%), while cases involving medication (n = 1130; 52%) showed an escalation from 12 to 211 calls/year (+ 1758%). Three hundred and seventeen (28%) of these cases were explicitly marked as medication errors (e.g., "mix-up") in the documentation by the PC staff. Within these accidental exposures involving medications the average number of involved drugs/case was 2.2 (max. 3.1 in 2012) compared to an average number of 1.4 in all cases of the PC. Overall in 1401 cases (65%) a non-medical management could be recommended as sufficient by the PC, and 813 cases (72%) focused on accidental exposures involving medication.
Conclusion: Enquiries from nursing homes are a disproportionately growing part of PC consultations mainly caused by a considerable increase in accidental medication errors and mix ups. In these cases the number of substances involved is above average, therefore these consultations are presumably more complex in considering interactions and risks. Nevertheless a non-medical treatment could be recommended in most cases. A high rate of cost-saving for the public health system can be assumed.

78. Plan C: Intra-muscular overdose of methotrexate. A rarely reported entity

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Objective: Methotrexate (MTX) is widely used in oncology, rheumatology, and gynecology. While toxicity from oral and intravenous administration is extensively described, complications from intramuscular (IM) injection for termination of pregnancy are rarely reported. We present a patient with an IM MTX overdose in which manifestations of toxicity were prevented by early recognition and prompt therapy.
Case report: A 22-year-old (1.67 m^2) woman with persistent serum beta-hCG elevations of approximately 90 mIU/mL for 5 weeks after taking a "morning after" pill was given MTX IM at a clinic. The intended dose was 50 mg/m^2. However, she received the entire bottle (250 mg), equivalent to 150 mg/m^2. The patient tolerated the medication well, but was sent to a hospital upon recognition of the error. Since there are limited data on the pharmacokinetics regarding IM MTX, she was given an equimolar dose of leucovorin prior to the return of the MTX concentration. Her laboratory evaluation, which included renal, hepatic, and hematologic functions, was normal. The patient received intravenous hydration and was started on oral leucovorin while awaiting the MTX concentration, which was later reported as 2.88 μmol/L, obtained at approximately 6 h post administration. Given this concentration, she was provided another dose of IV leucovorin approximately 24 h post administration, at which time a concentration of 0.05 μmol/L (below level of toxicity) ultimately returned. She remained asymptomatic, and her repeat laboratory results remained normal. After the completion of IV leucovorin, she was discharged home with weekly follow ups. She remained asymptomatic over the next 4 weeks, with normal laboratory values.
Conclusion: Severe toxicity following IM MTX overdose has been reported to result in stomatitis, renal failure, and pancytopenia.[1] However, in our case, early antidotal treatment with equimolar IV leucovorin administration may have prevented these manifestations of toxicity. Given the limited data on the pharmacokinetics and pharmacodynamics in the setting of IM MTX overdose, treating IM MTX overdose similar to an IV MTX overdose is safe and effective.

Reference

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79. Iatrogenic recombinant factor VIII overdose in a patient with hemophilia A

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Objective: Recombinant Factor VIII (rFVIII) is the standard treatment for bleeding episodes in patients with hemophilia A. Iatrogenic overdose of rFVIII is not previously documented in the literature. We report a unique error involving a child with known hemophilia A who received an iatrogenic overdose of rFVIII.
Case report: A 3-year-old (16 kg) boy with a history of severe hemophilia A presented to the emergency department (ED) following a spontaneous left knee hemarthrosis. His pre-treatment Factor VIII activity was less than 0.2%. Following consultation with a pediatric hematologist, the child was ordered rFVIII, 30 IU per kg (total = 500 IU) intravenously (IV) to increase his Factor VIII activity to greater than 50%. A medication error was made and instead of receiving 500 IU total dose, 500 IU per kg was administered, for a total dose of 8000 IU rFVIII. Factor VIII activity obtained 12 h after the administration of rFVIII was 65% and at 36 h was 19%. The child did not develop any thrombotic consequences of the rFVIII overdose.
Conclusion: Massive iatrogenic rFVIII overdose in a patient with hemophilia A did not result in an increase in his Factor VIII activity to the expected degree and he did not develop any thrombotic complications. Given that each IU rFVIII administered per kilogram body weight is expected to increase the Factor VIII activity by 2%, the expected Factor VIII activity increase in this patient was 1000%. By history, the patient had previously been treated with rFVIII, therefore it is possible that the child had developed antibodies to the treatment.

80. Pharmacogenomic testing to mitigate azathioprine adverse drug effects

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Objective: 1) Describe two cases of neutropenia following initiation of azathioprine therapy in patients with thiopurine S-methyl transferase (TPMT) polymorphisms. 2) Describe the role of pharmacogenomics in modern toxicology and how its application can be used to limit adverse drug reactions (ADR).
Case series: Azathioprine, and its metabolite 6-mercaptopurine, is a thiopurine used in the treatment of inflammatory bowel disease and in post-transplant patients. Thiopurines undergo a complex metabolism that is governed by several enzymes, including TPMT, to produce the active drug 6-thioguanine nucleotide (6-TGN). Individuals with specific polymorphisms within the TPMT gene are at increased risk of developing toxic levels of 6-TGN (>450 pmol/8×10^8 RBC) and inducing subsequent myelosuppression. We describe two cases of neutropenia in post-renal transplant patients receiving azathioprine. Patient IB is a 17-year-old male with a history of atypical hemolytic uremic syndrome requiring two renal transplants done 10 years apart. While on azathioprine, IB became neutropenic with an absolute neutrophil count (ANC) of 370 μg/L requiring granulocyte-colony-stimulating factor (GCSF). Azathioprine was discontinued and neutrophil counts increased. TPMT genotyping revealed *1/*3A haplotype, consistent with reduced TPMT enzyme activity. AZA-metabolite 6-TGN was elevated (955 pmole/8×10^8 red blood cells (RBC) initially, then 500 pmole/8×10^8 RBC once drug held), suggesting that the patient's myelosuppression was due to toxic accumulation of 6-TGN. Patient XG is a 7-year-old boy born with congenital nephrotic syndrome that progressed to end-stage renal disease necessitating a deceased donor renal transplant. Five years later, XG was started on azathioprine and rituximab. Soon after, he became neutropenic with an ANC of 0. TPMT genotyping was sent and the patient was found to have the *1/*3C haplotype, indicating reduced TPMT enzyme activity. Interestingly, AZA metabolite 6-TGN was normal and 6-MMPN was below detection limit.
Conclusion: ADRs are estimated to result in thousands of deaths worldwide on an annual basis; genetic variability has been reported to be responsible for up to 50% of ADRs. The polymorphisms of azathioprine metabolism demonstrate the importance of identification of clinically significant variants that can improve dosing, provision of genotype data at the time of prescribing, and integration within electronic medical record systems.[1]

Reference

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81. Clinical outcomes of methylphenidate intoxications in children and adults: A prospective follow-up study

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Objective: Methylphenidate (MPH) is a stimulant drug used in treating Attention Deficit Hyperactivity Disorder (ADHD). The number of MPH prescriptions in the Netherlands has substantially increased in recent years as has the number of inquiries regarding MPH at the Dutch Poisons Information Center (DPIC). The purpose of this study was to investigate whether the current Dutch guideline for hospital referral in case of overdose (MPH dose ≥ 2 mg/kg), is justified. Moreover, patient characteristics and exposure circumstances were investigated.
Methods: We performed a prospective follow-up study on MPH exposures reported to the DPIC (August 2012–August 2013). Patients and physicians were interviewed by telephone using standardized questionnaires. Three physicians of the DPIC independently assessed the severity of symptoms of each patient as none/mild (observation at home) or moderate/severe (hospital referral). Receiver operating characteristic (ROC) analyses were used to determine the optimal dose threshold for hospital referral. This study was approved by the Medical Ethics Committee of the University Medical Center Utrecht.

Results: 364 physicians and/or patients were interviewed. Half of all inquiries concerned children < 18 years. Accidental exposures (40%) mostly occurred at home involving the patient's own medication or that of a family member. Compared to accidentally exposed patients, intentionally exposed patients were exposed to higher MPH doses (3.1 vs. 1.6 mg/kg), more often used immediate release MPH formulations (62 vs. 30%), and more frequently had concomitant exposures (71 vs. 17%). Primary motives for intentional MPH exposures were suicide attempts, "to feel good" and "to reduce hyperactivity". In fourteen patients, MPH was "sniffed". In patients exposed to MPH without concomitant exposures, the most commonly reported symptoms were agitation, sleepiness, tachycardia, dry mucosa, and headache. No severe symptoms such as convulsions, cardiac arrest or coma were reported. The severity of clinical effects increased at doses > 3 mg/kg, e.g., above this dose level, hallucinations or psychosis were occasionally reported.
Conclusion: We propose to increase our current dose threshold for hospital referral from 2 to 3 mg/kg or at lower doses when clinical signs indicate the need for referral. Application of this new dose threshold will reduce unnecessary hospital referral, thereby reducing costs without jeopardizing patient safety.

82. Pregabalin and gabapentin abuse and toxicity as disclosed from postmortem cases

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Objective: Pregabalin (PRG) and gabapentin (GBP) are gamma-aminobutyric acid analogues used for treating neuropathic pain and partial seizures. There has been increasing concern about the abuse potential of PRG.[1] PRG may have a higher addiction potential than GBP due to its rapid absorption and faster onset of action. Our objective is to estimate the proportion of PRG and GBP abuse cases in all PRG and GBP fatalities.
Methods: We investigated all deaths in Finland in which PRG or GBP was found in postmortem toxicology during 2010–2011. There were 101,472 deaths, and a medico-legal autopsy was performed in 22,421 cases. PRG was found in 316 and GBP in 43 cases. We investigated all the laboratory findings, death certificates and forensic pathologists' referrals in each case to estimate if PRG or GBP had been abused
Results: Drug abuse was associated with 48.1% of the PRG and 18.6% of the GBP findings. The proportion of fatal PRG poisonings to all PRG findings was 9.2%, while this figure was 4.7% for GBP. In the drug abuser cases, the proportion of fatal poisonings was 19.1% and 12.5% for PRG and GBP, respectively. The median blood concentration of PRG was 15 mg/L in the abuser group and 5.8 mg/L in the other cases. For GBP, the medians were 12 mg/L and 8.3 mg/L, respectively. Additional opioid use was found in 91.4% of the PRG abuse cases and 87.5% of the GBP abuse cases.
Conclusion: Nearly a half of the deceased with a positive PRG finding were drug abusers, but less than a fifth of the GBP use was abuse. Patients have survived severe PRG poisonings in medical treatment, but the outcome of PRG abuse can be fatal, especially when combined with opioids. PRG should be considered and classified as a benzodiazepine-like drug with a considerable abuse potential. In our material, GBP findings were more infrequent and GBP had substantially less abuse potential than PRG.

Reference

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83. Specific aspects of acute poisoning with new psychoactive substances in adolescents in a pediatric poisoning center

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Objective: To assess the incidence and characteristics of poisoning with new psychoactive substances in a Pediatric Poisoning Centre.
Methods: We performed a retrospective study of cases with new psychoactive drug poisoning admitted to our center during a 3-year period. The following criteria were taken into consideration: incriminated product, age, gender, symptoms, modality and place of poisoning
Results: Out of the 137 patients with drug abuse poisoning admitted between 1 November 2009 and 1 November 2012, 119 cases were registered with novel psychoactive drug poisoning. Distribution of the number of cases was the following: 59 patients in the first year, 42 in the second year and 18 in the third year. We noted the association of novel psychoactive drugs with: alcohol in 11 cases, medicines in 9 cases, medicines and alcohol in 2 cases and heroin in 4 cases. The main symptoms were: dizziness, vertigo, somnolence, confusion. Coma was reported in 4 patients and cardiac disturbances in 2 patients. The patients' average age was 15.6 years and 64% were boys. Out of the total cases 98% appeared in urban area in clubs and private parties. The average length of stay was 1.5 days and no deaths occurred. The implicated products were unknown in 38% of patients.
Conclusion: The number of new psychoactive substance poisonings in adolescents significantly decreased in 2012 due to governmental measures (closing the specific stores). Severe symptoms such as coma or cardiac disturbances were rarely noted in occasional consumption in adolescents.

84. Mild valproic acid poisoning and development of near fatal cerebral edema

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Objective: Valproic acid (VPA) poisoning has been associated with fatal cerebral edema (CE) when intoxication is severe (VPA > 480 μg/mL). Severe CE ensued despite aggressive

therapy in a case of mixed overdose that included VPA which peaked at only 162 µg/mL.

Case report: A 17-year-old black male with a mood disorder ingested sustained release VPA 146 mg/kg, olanzapine 2.9 mg/kg, imipramine 1.9 mg/kg and guanifacine 0.39 mg/kg. No drug other than VPA is known to cause CE. Combativeness in the emergency department prompted endotracheal intubation. At 1.5 h post-ingestion (PI), VPA peaked at 162 µg/mL. At 11 h PI, VPA and ammonia were 141 µg/mL and 47 µmol/L, respectively. Levocarnitine 50 mg/kg/dose intravenously was administered every 4 h beginning at hour 17 PI. At 23 h PI, VPA fell to 119 µg/mL but ammonia increased to 705 µmol/L. Urine assay for organic acids was positive for VPA metabolites. Head computed tomography (CT) was normal. Hemodialysis (HD) was performed for 3 hours. Post-dialysis VPA was 80.4 µg/mL and ammonia was 411 µmol/L. Levocarnitine dose was decreased between hours 43 and 67 PI and discontinued when VPA was 56 µg/mL and ammonia was 31 µmol/L. At 63 h PI, systemic hypertension prompted head CT which showed diffuse CE with impending brain herniation. Hypertonic mannitol and saline 3% were initiated. Intracranial pressure (ICP) monitoring revealed an initial pressure of 17 mmHg. Repeat head CT 4.5 h after initiation of hypertonic therapy demonstrated markedly improved CE. ICP remained <23 mmHg over the next 7 days, allowing gradual withdrawal of hypertonic saline. Ventilator-associated pneumonia complicated his course; extubation was successful on day 11. At 26 days PI cognitive and motor function were normal.

Conclusion: This ingestion demonstrates that despite treatment with levocarnitine and HD, a relatively small dose VPA ingestion with co-ingestion of olanzapine, imipramine and guanifacine caused moderate hyperammonemia and life-threatening cerebral edema 63 h PI. Hypertonic therapy resulted in resolution of intracranial hypertension and rapid improvement in CE on head CT. The timing of this intracranial complication suggests a role for neurotoxic metabolites of VPA in the generation of CE in this patient.

85. Therapeutic drug monitoring of clozapine and norclozapine using a multidrug ultra-high performance liquid chromatography-tandem mass spectrometric method

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Objective: Therapeutic drug monitoring (TDM) is of great importance for drugs with a high interindividual variability in serum concentration, a narrow therapeutic range or serious toxic side effects. Clozapine, an atypical antipsychotic, meets these requirements. According to the Arbeitsgemeinschaft fur Neuropsychopharmakologie und Pharmakopsychiatrie (AGNP)-TDM consensus guidelines, TDM of clozapine and its metabolite norclozapine is strongly recommended.[1] Three hundred and thirty serum samples, sent to the toxicological laboratory of Ziekenhuis Netwerk Antwerpen for monitoring of clozapine, were tested with a new ultra-high performance liquid chromatography-tandem mass spectrometric method (UHPLC-MS/MS). The aim of this research was to evaluate this method for TDM of clozapine and norclozapine, but also to determine other antipsychotics present in these serum samples. The obtained serum concentrations were interpreted based on the therapeutic ranges defined by the AGNP group.[1]

Method: As recommended for TDM, serum samples were taken just prior to the morning dose of the antipsychotic (trough concentration). After routine analysis, the remainder of the serum samples were sent to the toxicological center of the University of Antwerp. All samples, after a simple liquid-liquid extraction with methyl t-butyl ether, were analyzed using a fully validated UHPLC-MS/MS method which is able to quantitate 16 different antipsychotics and 8 of their major metabolites.

Results: 323 of the 330 serum samples contained clozapine and norclozapine. For clozapine, only 21.8% of the serum concentrations were within the therapeutic range of 350–600 ng/mL. For norclozapine, 67.0% were within the therapeutic range. Other antipsychotics found and the percentages of samples within the therapeutic range were: amisulpride (n = 29, 20.7%), aripiprazole (n = 38, 52.6%), dehydro-aripiprazole (n = 40, 12.5%), bromperidol (n = 6, 0.0%), haloperidol (n = 37, 81.1%), olanzapine (n = 19, 52.6%), norolanzapine (n = 16, 25.0%), paliperidone (n = 86, 49.1%), pipamperone (n = 8, 50.0%), risperidone (n = 16, 62.5%), quetiapine (n = 55, 49.1%), 7-hydroxy N-desalkylquetiapine (n = 51, 94.1%), and zuclopenthixol (n = 21, 57.1%).

Conclusion: The retrospective analysis of 330 serum samples revealed that for most of the antipsychotics found the serum concentration was outside of the proposed therapeutic range. However, correlation with the dose and clinical effect is necessary for interpretation.

Reference

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86. Psychomotor agitation in acute poisoning: Could we call it a toxidrome?

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Objective: Psychomotor agitation (PA) is a poorly defined but very common condition presenting as an important issue in the emergency department (ED) and can be considered a toxidrome due to its frequent association with acute poisoning. To define the particularities of acute poisoning with PA we have evaluated the differences between agitated (AC) and non-agitated (NAC) acute poisoning cases attending our ED in the last 5 years (2008–2012) to stress the particular characteristics of the agitated subgroup.

Methods: Based on the files of our data base, gathered in a prospective way, we have compared the clinical, epidemiological and analytical data and therapeutic approach of AC and NAC acute poisoning patients.

Results: The total number of toxic cases was 5341 (1% of the total ED cases). Agitation was found in 522 (9.8%). Men were more prevalent in total cases (62.4%) and in AC (66.0%) but

there were no significant gender differences between AC and NAC. Agitation was significantly more frequent in the 20–40 years age group ($p < 0.001$). Recreational overdoses were clearly overrepresented (68.1% in AC vs 52.9% in NAC) by comparison with suicides and accidents ($p < 0.001$). There were no significant differences between NAC and AC in relation to the causal agent, although agitation was more frequent in drugs of abuse cases. In the ethanol group with analytical results (total cases 2227/AC 293) the agitation incidence was higher than expected in the groups with a blood ethanol concentration ranging from 0 to 0.5 g/L and from 3 to 4 g/L ($p < 0.01$). It confirms that the agitation effect is not dose-dependent in acute ethanol cases and even appears when a sedative effect would be expected. There were more signs and symptoms from the adrenergic axis in the AC and treatment was focused on sedation procedures, mainly benzodiazepines.

Conclusion: Psychomotor agitation was present in 10% of acute poisonings; it was more prevalent in young adults and was associated with recreational overdoses. In cases involving ethanol it was independent of the dose. It was associated with a higher number of signs and symptoms and treatment is specifically addressed towards sedation.

87. Gabapentin overdose: A case series

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Objective: The purpose of the study was to assess the toxicity and clinical feature of gabapentin in overdose, because there is little information in literature on this topic.

Methods: Cases of overdose of gabapentin from eight poisons information centers in Austria, Germany, and Switzerland were analysed retrospectively. Inclusion criteria were monointoxication, defined dose, and documented follow-up. Severity of symptoms was assessed according to the Poisoning Severity Score.

Results: A total of 48 cases met the inclusion criteria. Eight patients were children (age 1.2–13 years), and 40 patients were adolescents or adults (age 15–84 years). Dose ranged from 300 to 9000 mg (8.3–500 mg/kg) in children and 600 to 60,000 mg in adolescents/adults. Six children remained asymptomatic, whereas in two cases mild or moderate symptoms were observed. Most adolescents/adults developed no or only mild symptoms (92%); only three patients suffered from moderate symptoms. Mild and moderate effects in adolescents/adults were caused by doses from 600 mg and 3000 mg, respectively. In contrast, adults tolerated doses up to 48,000 mg without adverse effects. Most frequent symptoms were fatigue (15%), somnolence (19%), sopor (4.3%), dizziness (8.5%), headache, tremor, ataxia, mild agitation, and abdominal pain (4.3% each). In single cases coma, tachycardia, bradyarrhythmia, atrioventricular block, and collapse were observed.

Conclusion: Overdose of gabapentin frequently resulted in altered mental status. In most cases only mild symptoms occurred. Severe symptoms were not observed. There was no clear correlation between dose and severity of symptoms. These results agree with case series described by other authors,[1,2] Nevertheless, for a comprehensive assessment of the toxicity of gabapentin further investigations are necessary.

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88. Diabetes insipidus associated with valproic acid overdose: A rare case of valproic acid toxicity

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Objective: Nephrogenic diabetes insipidus (DI) is caused by a number of medications including foscarnet, clozapine, and most commonly lithium. Currently, there are no reports in the English literature that describes valproic acid (VPA) induced nephrogenic DI. Here we present a case of DI associated with VPA overdose.

Case report: A 53-year-old man with a past medical history of schizophrenia and bipolar disorder taking VPA, benztropine, clonazepam, and fluphenazine presented to the emergency department (ED) about 4 h after taking approximately 90 of his 500 mg extended release VPA (divalproex sodium) tablets and 15 of his 2 mg benztropine tablets in a suicide attempt. Upon arrival, he was alert but mildly agitated and complained of polyuria. His initial vital signs were; blood pressure, 151/75 mmHg; heart rate, 80/min; respirations, 20/min; oxygen saturation, 98% on room air; and afebrile. While in the ED, he became very lethargic and required intubation. The serum sodium was 151 mEq/L, ammonia 24 μmol/L, lithium < 0.2 mmol/L and VPA 733 mg/L, for which L-carnitine was administered intravenously. The patient received a total of 3.5 L of normal saline in the ED and he put out over 8.4 L of dilute urine. His serum osmolality was 309 mOsm/kg and urine osmolality was 128 mOsm/kg. The sodium and VPA level peaked at 165 mEq/L and 752 mg/L, respectively. The patient continued to produce a large amount of urine – 18.4 L over 24 h. He was treated with desmopressin without response and 5% dextrose with half-normal saline supplementation – 21.5 L over 24 h. Head computed tomography and chest X-ray did not show any abnormalities. His serum and urine osmolality and the other laboratory abnormalities normalized over the course of 2 days.

Conclusion: Although VPA has never been reported to produce nephrogenic DI, there is growing evidence of VPA inducing renal tubular dysfunction.[1] Nephrogenic DI may be considered as a rare but important effect that can be seen in patients with severe VPA overdoses.

Reference

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89. Bupropion and ethanol co-ingestion presenting with hypotension and focal seizure activity

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Objective: Describe a case of bupropion toxicity resulting in hypotension and focal seizure activity in the absence of sodium channel blockade.
Case report: A 33-year-old woman with a history of depression and alcohol abuse was found at home with altered mental status and empty bottles of an extended-release formulation of bupropion and gabapentin. She was brought to an outside hospital emergency department (ED) where she was noted to have seizure-like movements. She received lorazepam and was intubated. She did not require sedation after intubation. Serum ethanol level was 228 mg/dL and the urine drug screen was positive for benzodiazepines and amphetamines. Arterial blood gas: pH 7.23, pCO_2 41 mmHg, bicarbonate 17 mmHg. Electrocardiogram (ECG) demonstrated normal sinus rhythm with QRS 94 ms and QTc 518 ms. She became hypotensive to 58/35 mmHg which did not improve with fluid resuscitation. Therefore, a dopamine infusion was initiated; norepinephrine was substituted for dopamine after transfer to the tertiary care center. Gas chromatography/mass spectrometry (GC/MS) urine drug screen detected bupropion, diazepam, and nicotine. She had a recurrence of seizure-like activity and received 2 mg of midazolam and was started on a propofol infusion She required vasopressor support with a norepinephrine infusion for 2 days. As propofol was weaned on hospital day (HD) 2, she was noted to have myoclonic activity. Electroencephalogram (EEG) demonstrated background beta and delta activity with several generalized poly-spike-and-wave discharges and several focal poly-spike-and-wave discharges over the right temporo-occipital region. Given the focal EEG findings, the patient was treated with lacosamide and valproic acid. Her hospital course was complicated by acute lung injury which delayed extubation until HD 9. She was discharged on HD 13 without sequelae.
Conclusion: Bupropion overdose can lead to hypotension and focal seizure activity in the absence of sodium channel blockade.

90. Methylphenidate poisoning: A devil in disguise?

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Objective: In March 2013 one fatal case of methylphenidate (MPH) poisoning was reported to the poison center (PC). Route of exposure was probably nasal application. Subsequently we decided to describe the epidemiology of methylphenidate poisoning with the focus on clinical presentations, route of exposure and severe cases.
Methods: Retrospective analysis of data collected by the PC between January 2000 and December 2012. Epidemiological analysis and description of all reported cases concerning methylphenidate. All reported cases with mono-intoxication and a successful follow up were reviewed and analysed subsequently in regard to clinical presentations and the poisoning severity score (PSS).
Results: In total 968 cases of methylphenidate poisoning were reported to the PC. There was a nearly linear increase in methylphenidate poisonings throughout the years with an overall escalation in the year 2007. During this time period furthermore a shift in the patients' age favoring patients older than 14 years was detected. Six hundred and nine cases with single substance intoxications were registered; 206 of them had successful follow-ups. Most of the cases showed none or mild clinical symptoms (PSS 1 or less). Only 17 cases with a PSS of 2 were reported. No cases of severe intoxications (PSS 3 or death) were found. Nine patients presented with an irregular (parenteral) administration route (nasal, intravenous (IV), subcutaneous).
Conclusion: Methylphenidate is a widely prescribed substance in children with a high potential for abuse in young adults. The number of intoxications reported to the PC was small but disproportionately increasing throughout the years. The course throughout the years reflects changes in prescription policies. Overall no severe intoxications were reported. In contrast to three cases reported in the literature[1–3] which showed a fatal outcome after abuse (nasal and IV) the oral ingestions were associated with only mild to moderate symptoms.

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91. A case of unintentional naltrexone-induced opioid withdrawal successfully treated with buprenorphine in an emergency department setting

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Objective: Naltrexone-induced opioid withdrawal is difficult to treat due to its long acting antagonism and high affinity for the μ-receptor. Escalating doses of full μ-agonists may provide partial relief at risk of bioaccumulation and subsequent respiratory depression. In naltrexone-induced rapid opioid detoxification regimens, partial μ-agonist, buprenorphine, has been reported to attenuate withdrawal symptoms.[1] We report a case of unintentional naltrexone-induced opioid withdrawal

successfully treated with buprenorphine in the emergency department (ED).

Case report: A 44-year-old woman receiving chronic opiates (30 mg morphine orally, four times per day (PO QID)) for fibromyalgia presented to the ED with myalgias, abdominal cramping, nausea, vomiting, diarrhea, hyperhidrosis, and fatigue. She ingested 50 mg naltrexone prescribed for constipation and within 30 min developed unremitting withdrawal symptoms. She appeared distressed with heart rate 84, blood pressure 101/68, temperature 35.8°C, respiratory rate 16, and SpO_2 99%. Laboratory studies showed a pH of 7.52, PCO_2 35, HCO_3 29, consistent with a mixed respiratory alkalosis and metabolic alkalosis. In the first 2 h 1 L 0.9% normal saline and 1 mg lorazepam intravenously were provided without relief. Buprenorphine (4 mg sublingually) was then provided and within 45 min symptoms resolved. After 5 h observation and no recurrence of symptoms she was discharged home.

Conclusion: Peripherally restricted μ-antagonists (subcutaneous methylnaltrexone or oral naloxone) are preferred for opioid-induced constipation, avoiding withdrawal symptoms. Central α2-adrenergic antagonists, benzodiazepines, and antiemetics may only provide partial relief of opioid withdrawal symptoms as they do not act at the μ-receptor, are unlikely to reduce opiate craving, and will likely require repeat dosing in withdrawal induced by long acting μ-antagonists (naltrexone). In contrast to full μ-agonists, partial agonist buprenorphine is long acting (12 h in 2 mg dose), slowly dissociates from the μ-receptor, less sedating, and produces less respiratory depression. In our case the clinical resolution of withdrawal suggests buprenorphine was successful at displacing naltrexone from the μ-receptor. Buprenorphine can successfully treat naltrexone-induced opioid withdrawal in the ED setting and should be considered if readily available.[2]

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92. Non-medical use of attention deficit hyperactivity disorder drugs by adults: A comparative study of atomoxetine versus methylphenidate

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Objective: Atomoxetine (ATM) is recommended as first line therapy for attention deficit hyperactivity disorder (ADHD) patients with a substantial history of drug abuse even though its abuse potential needs to be qualified. The proportion of patients receiving ATM as first line therapy increased from 4% in 2009 to 11% in 2011.[1] The purpose of this study was to investigate the relationship between non-medical and therapeutic use of ATM, the motivation behind it, and how this compares to methylphenidate (MPH).

Methods: This is a retrospective observational analytical study of ADHD drug exposure (ATM and MPH) in adults (> 18 years of age) reported to the Danish Poison Information Centre in the period January 2006 to June 2012. Data on therapeutic use was provided by the Danish National Board of Health (2007–2012).

Results: The study included 28 ATM and 394 MPH enquiries. Median age and interquartile range: 22 year (18–28 year) for ATM, 27 year (20–35 year) for MPH (2 unknown cases). Females/males: 11/17 for ATM, 168/225 for MPH (1 unknown case). Cases with/without prescriptions: 13/5 for ATM (10 unknown cases), 163/86 for MPH (245 unknown cases). The proportion of exposures motivated by recreational drug use was significantly lower for ATM (19%) than for MPH (40%) ($z = .14$, $p = 0.032$). Enquiries per 1000 therapeutic users were 0.001 for ATM ($r^2 = 0.59$, $p = 0.13$), and 0.004 for MPH ($r^2 = 0.98$, $p = 0.0008$). The relationship between enquiries and therapeutic use was significantly less strong for ATM than for MPH ($F = 10.40$, $p = 0.018$).

Conclusion: These results suggest that ATM is less likely than MPH to be used for non-medical purposes, and that ATM exposures are less likely motivated by recreational purpose.

Reference

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93. Fifty years of the German National Committee for the Assessment of Poisonings

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Background: The German National Committee for the Assessment of Poisonings located at the Federal Institute for Risk Assessment (BfR) is now looking back on 50 years of successful prevention work. It was established in 1964, within the former German Health Authority (BGA), modelled on the American Food and Drug Administration (FDA) committee "National Clearinghouse for Poison Control Centers", together with the contemporary BfR Centre for Documentation and Assessment of Poisonings. Likewise, poison information centers (PCs) were established in the German federal Länder according to the American model. Renowned experts were appointed to the Committee who supported the German PCs' services in consultancy and treatment in cases of accidents

Results: Owing to the individual and appropriate treatment of cases of poisoning in cooperation with the poison information and treatment centers, decisive improvements have been achieved regarding treatment prevention and consumer protection (e.g., new product compositions, warning labels and bans on sales) leading to a drastic reduction in fatal poisoning accidents in children. The Committee, in which more than 190 experts have collaborated up to now, provides input for legislative procedures.

For instance, with the backing of the Committee, BfR proposed the EU-wide restriction of the sale of paraffin-containing, colored and perfumed lamp oils, which led to a marked drop in the number of poisoning accidents involving such oils. Also, the EU standard on child-resistant closures, the restrictions on methanol in consumer preparations as well as changes to formulations and warnings on mechanical dishwashing products are all down to the initiative of Committee members. The Committee has evaluated information on the identification and treatment of poisonings since 1965. It stores such information within BfR in a "poison information and recording system – GIFAS". Besides substance and treatment information, details on more than 500,000 formulations, 100,000 cases of poisoning and more than 900 detailed human case reports (German/English) have been processed.

Conclusion: The most important goal of the Committee's work in the future is the setting up of an annual national monitoring report of poisonings in cooperation with the German PCs and the Society for Clinical Toxicology.

94. The Ljubljana Poison Control Center 40 years on

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Objective: With a population of 2 million Slovenia lies in Central and South-eastern Europe, touching the Alps and bordering the Mediterranean. The country's only poison control center (PCC) is located in Ljubljana, the largest town with 280,000 inhabitants.

Methods: Historical presentation and description of the Ljubljana PCC.

Results: The first written documents concerning the need for a PCC in Slovenia go back to 1962. In 1973 the PCC with its own toxicology ward was established as a part of the Division of Internal Medicine at the Ljubljana University Medical Center. Initially, the PCC employed three specialists in internal medicine who treated poisoned patients and performed a toxicology consulting service for other physicians. In 2013 it still forms a part of the Division of Internal Medicine and employs five internal medicine specialists, two registered nurses, nine nurses and a secretary. The PCC has a renovated ward with nine beds located above the Medical Emergency Department and Intensive Care Unit where 200 poisoned patients are treated per year. The clinical toxicologists work at the Emergency Department and offer clinical consultations with intensivists. They also provide a 24/7 clinical toxicology consulting service to all physicians and other experts in Slovenia, but not to the general public. Annually they respond to approximately 2000 calls and type them into a Cloud database accessed over the Internet. The Slovenian Register of Intoxication, in which all poisonings have to be reported on a special form, is also located in the PCC. Both databases are connected to business intelligence software that provides reports and analysis on poisonings in Slovenia. The PCC also houses the most important antidotes, which can be sent immediately to other hospitals and neighboring countries if necessary. Furthermore, it maintains a Slovenian register of antidotes and antidote stores in Slovenia. PCC physicians are teachers and researchers at the University of Ljubljana Faculty of Medicine and organize preventive campaigns for the general public.

Conclusion: With 40 years practice in clinical toxicology the PCC's clinical experience and information consulting expertise has produced impressive results.

95. Setting up and stages of toxicological service work in the Sverdlovsk region: 40 years of toxicological service work in the Russian Federation

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Objective: In the Sverdlovsk region of Russia a special medical service for patients with poisoning was set up in 1973 due to the high incidence of chemical poisoning among the population and the increasing number of unfavorable outcomes. This study analysed the process of setting up the toxicological service in a large industrial region of Russia.

Methods: Documents of the Ministry of Health Affairs of the region, the ambulance service, toxicological departments and the forensic service bureaus were examined

Results: In 2013 the service involved in the treatment of poisoning in Sverdlovsk had operated for 40 years. In the development of this service, we can distinguish several stages. A special medical service to patients with acute poisoning started work in Yekaterinburg (the region's administrative center) in 1967. At that time the first toxicological brigade was formed as part of the ambulance service. This was followed by the organization of a special treatment center for acute poisoning (1973–1989). In 1991 the next stage in the development of this service started. The earlier treatment center of poisoning became a center of poisoning for Sverdlovsk city only, alongside a regional center. In addition four toxicological departments in other large cities of the region were opened. During some years, there was an organized mobile brigade for the treatment of patients in the territory of Sverdlovsk region. In the structure of the medical catastrophe center a system of toxicological monitoring in cases of acute intoxication was developed. Mortality in the centers is currently 2.5–3.5%. We managed to stabilize the morbidity to the level of 160–180 cases per 100 thousand population. The mortality from acute intoxication in the Sverdlovsk region is approximately two times lower than in the rest of Russia. The next stage was the opening of the department of clinical toxicology in the Ural State Medical University (1995). The department provides clinical toxicologists for the Urals and Siberia. Since opening 3184 doctors have been trained.

Conclusion: In the Sverdlovsk region of Russia the service for the treatment of acute poisoning has grown and expanded. It goes without saying that the service needs further development.

96. Comparison of 15,329 unit dose and 12,599 non-unit dose pediatric laundry detergent exposures using US National Poison Data System data: 2012–2013

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Objective: Toxicity from unit dose laundry detergents (UD) has been reported in Europe and the US. We compared pediatric exposures to UD and non-UD laundry detergents (NUD) in the US since their marketing in 2012.
Methods: Start date, route, medical outcome, clinical effects (CE), and therapies for pediatric (0–5 years), closed, human, single substance exposures to UD and NUD products in US National Poison Data System (NPDS) (1 January 2012 through 31 October 2013) were compared by likelihood ratio Chi-square and Fisher's exact (SAS JMP 9.0.0). Exposure time courses were correlated (r) to Internet searches using Google Trends (GT)
Results: 15,329 UD (15,116 liquid, 142 granular, 71 liquid-granular) and 12,599 NUD exposures were compared. Frequency of UD exposures increased from 0 to approximately 30/day while NUD exposures decreased from approximately 22 to approximately 17/day. UD exposures best correlated with GT searches 3 weeks earlier ($r = 0.713$), although the first UD exposure was 3 weeks before the first GT search. Aspiration and ocular exposures were more likely for UD (<0.001, Fisher's exact). For the 57 CEs reported for >8 subjects; odds ratio (UD:NUD) was >1 for 55, p-value (Fisher's exact) was < 0.05 for 47 (Table 1). For the 18 treatments reported by >8 subjects: odds ratio was >1 for 16, p value was <0.05 for 13. Exposure to UD was more likely to be associated with Major/Fatal and Moderate/Major/Fatal outcomes ($p < 0.0001$).
Conclusion: Pediatric UD exposures have increased significantly since their 2012 release in the US. Exposure to UD products is associated with increased clinical effects, therapeutic interventions and more serious outcomes.

97. Surveillance of biocide-related toxic exposures in Italy

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Objectives: European legislation concerning the placing on the market of biocidal products (Directive 98/8/EC; Regulation 528/2012/

Table 1. Comparison of unit dose and non-unit dose pediatric laundry detergent exposures.

Category / Parameter	Odds ratio UD/LD	Unit dose (N = 15,329) Number	Unit dose (N = 15,329) Percent	Non-unit dose (N = 12,599) Number	Non-unit dose (N = 12,599) Percent	Chi square (likelihood ratio)	P value (Fisher's exact)
Route of exposure							
Aspiration	4.86	71	0.46	12	0.10	35.8	<.0001
Ocular	1.34	2108	13.8	1294	10.3	79.2	<.0001
Ingestion	0.99	13813	90.1	11460	91.0	5.82	0.9925
Clinical effects							
Pneumonitis	26.3	32	0.21	1	0.01	31.1	<0.0001
Esophageal injury	18.1	22	0.14	1	0.01	19.8	<0.0001
Coma	10.3	25	0.16	2	0.02	18.9	<0.0001
Respiratory Depression	8.90	65	0.42	6	0.05	46.5	<0.0001
Acidosis	6.74	41	0.27	5	0.04	25.6	<0.0001
Drowsiness/Lethargy	5.91	1072	6.99	149	1.18	642	<0.0001
Dyspnea	5.06	191	1.25	31	0.25	99.7	<0.0001
Bronchospasm	4.97	139	0.91	23	0.18	71.4	<0.0001
Excess secretions	3.10	253	1.65	67	0.53	82.7	<0.0001
Diarrhea	2.68	303	1.98	93	0.74	81.0	<0.0001
Cough/choke	2.56	2074	13.5	667	5.29	560	<0.0001
Vomiting	2.27	7370	48.1	2666	21.2	2245	<0.0001
Treatments administered							
Ventilator	9.98	85	0.55	7	0.06	63.8	<0.0001
Intubation	9.35	91	0.59	8	0.06	66.5	<0.0001
Oxygen	6.99	170	1.11	20	0.16	109	<0.0001
Antiemetics	4.66	210	1.37	37	0.29	103	<0.0001
Fluids IV	4.61	331	2.16	59	0.47	162	<0.0001
Bronchodilators	4.11	150	0.98	30	0.24	65.9	<0.0001
Steroids	3.60	140	0.91	32	0.25	53.9	<0.0001
Antibiotics	2.93	360	2.35	101	0.80	110	<0.0001
Medical outcome							
Fatal	–	1	0.0001	0	0	1.20	0.5489
Major/Fatal	6.51	95	0.0062	12	0.0010	58.2	<0.0001
Moderate/Major/Fatal	3.14	1167	0.0761	305	0.0242	403	<0.0001

EU) requires that Member States (MSs) report to the Commission information on poisoning incidents. In order to comply with this commitment, the Italian National Institute of Health and the National Poison Control Centre in Milan (NPCCM) implemented the Italian Surveillance System of Biocide-related Hazardous Exposures and Poisonings (SBHEP). The present contribution is aimed at characterizing cases of exposure to biocides occurred in Italy in 2007–2010.
Methods: Information on cases notified to SBHEP was reviewed and classified according to the Main Group of use and Product Type of the involved biocides. Active ingredients were grouped according to chemical class and identified by standard denomination. Each case was reviewed in order to evaluate the association between exposure and clinical effects and classified according to the Poisoning Severity Score.[1]
Results: In the period under study 6,210 human cases of exposure were identified. Some 26% (No. 2183) developed at least one sign/symptom possibly related to biocides. Severity of clinical effects was low in the vast majority of biocide-related poisonings (86%, No. 1486), moderate in 11% (No. 272). Twenty-seven cases suffered severe effects (1%). Most patients were exposed at home (76%, No. 1267). Occupational and environmental exposures were reported for 10% (No. 160) and 14% (No. 227) of cases, respectively. About 24% (No. 419) of cases were aged < 5 years. About 48% of cases were exposed to disinfectants (low severity: 810 cases; moderate severity: 149; severe: 11 cases); 5% to preservatives (low severity: 107 cases; moderate severity: 9; severe: 1 case); 46% to pest control (low severity: 883 cases; moderate severity: 114; severe: 15 cases).
Conclusion: Surveillance of biocide-related poisoning can provide a relevant contribution to prevention. Poison control centers should be considered as main sources of data at national level. However, common rules for data classification and reporting are urgently needed at European level in order to facilitate data comparison on biocide toxic exposures and highlight emerging problems.

Reference

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98. A preliminary comparison between human exposure cases identified in the US by the National Poison Data System and in Italy by the National System for Surveillance of Toxic Exposures and Poisonings

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Objective: The US National Poison Data System (NPDS) and the Italian National System for Surveillance of Toxic Exposures and Poisonings (NS-STEP) use similar methodologies for classification and analyses of poison center (PC) calls. A systematic comparison between the observations provided by these systems could highlight common emerging problems, encourage data sharing, analyses, and support prevention.

Table 1. Percentages of exposures by substance categories most frequently identified by the US and the Italian systems.

	ALL ages (%)		0–5 years (%)		> 20 years (%)	
	NPDS	NS-STEP	NPDS	NS-STEP	NPDS	NS-STEP
Analgesics	10	7	10	7	13	6
Cosmetics/personal care products	8	4	13	8	3	2
Household cleaning substances	7	17	20	9	6	17
Sedatives/hypnotics/ antipsychotics	6	10	1	2	11	21
Foreign bodies/toys	4	5	7	10	1	1
Topical preparations	4	2	7	2	2	3
Antidepressants	4	5	1	1	6	10

Methods: We performed an indirect comparison of the main characteristics of 2008 human exposure cases in the US and Italy as shown in NPDS and NS-STEP reports.[1,2]
Results: NPDS human exposures per thousand population were ten times higher than NS-STEP (8.00 vs. 0.77). For most of the US calls (93%) a PC was consulted from the exposure site, while in Italy 56% of calls were made from a hospital. In both countries most of cases were home exposures (91%, US and 93%, Italy, respectively) and most of exposures were unintentional (US: 83%; Italy: 78%). Patients aged 0–5 years were 52% in the US and 44% in Italy. About 54% and 48% of the American cases were exposed to pharmaceuticals and non-pharmaceuticals, respectively, while 40% of the Italian calls were pharmaceutical exposures, 57% to non-pharmaceuticals, 2% to both agents and 1% to unknown agents. Table 1 compares the percentages of exposures by substance categories most frequently identified by the US and the Italian Systems.
Conclusion: International monitoring and outbreak detection for poisoning public health events is needed. Study of international trends and data harmonization is required.

99. Surveillance of hazardous exposures to electronic cigarettes in Italy

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Objectives: Liquid solutions (e-liquids) used in electronic cigarettes (e-cigarettes) represent a potential source of toxic exposures to nicotine. This study provides a description of human exposures to e-liquids reported to the Italian National Poison Control Centre in Milan (INPCCM) in 2010–2013.
Methods: The INPCCM database was searched to identify human cases exposed to e-liquid from January 2010 through June 2013. Each case of interest was reviewed and classified according to the Poisoning Severity Score.[1]
Results: A total of 185 cases were identified. One case was reported in 2010 and 2011, respectively, 42 cases in 2012,

and 143 during the first 6 months of 2013. Some 15% of cases were aged 5 years or less, 7% 6–19 years, 64% 20–49 years, and 11% 50 years or more. About 58% of cases were men and 41% women. Most of the exposures were unintentional (96%) and occurred while the victim was using an e-cigarette (78%). Uncontrolled access to e-liquid by a young child accounted for 16% of cases, while 4% were victims of therapeutic error due to exchanging a cartridge with a pharmaceutical mono-dose preparation. Two cases developed allergic reactions. Intentional exposure occurred in 3% of cases including two cases of suicide attempt and three cases of abuse. The route of exposure was 80% ingestion, 9% inhalation and ocular, respectively, 4% dermal. About 38% of cases developed signs/symptoms possibly related to e-liquid exposure. Clinical effects most frequently reported were oropharyngeal irritation (10%), nausea (7%), ocular irritation (6%), vomiting (5%). In all symptomatic cases severity of medical outcomes was minor, but in two cases it was moderate. These last ones included: a 2-year-old child who developed ataxia, vomiting, and tachycardia following ingestion of a 3.6% nicotine solution; a 34-year-old patient who suffered headache, vertigo, gastric pyrosis, and dyspnea following unintentional e-liquid ingestion while inhaling from an e-cigarette.
Conclusion: Although most of the reported exposures did not have serious outcomes, it should be considered that e-liquids containing high nicotine concentrations may pose a serious health threat especially to children.

Reference

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100. Snus vs. cigarettes: A change in pattern of calls to the Norwegian poisons information center

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Objectives: Snus is a moist powder tobacco product popular in Sweden and Norway but banned in the rest of Europe. This nicotine product is put under the lip and through which the nicotine is absorbed. We report new trends in tobacco inquiries at the poisons information center and how these trends reflect on public health issues.
Method: Analysis of the poisons information database and Statistics Norway (SSB).
Results: The use of snus has increased in Norway during the past 10 years. At the same time cigarette smoking has decreased. The Norwegian poison center has registered a change in inquiries about accidental ingestion of snus vs. cigarettes in the same period. While inquiries about accidental cigarette ingestions dominated just a few years ago, snus inquiries are by far more frequent at the moment. In the statistics we find that cigarettes and snus have practically changed places. The total number of calls about unintentional ingestion of tobacco products has not changed over the years. They are quite stable, approximately around 450 with a range from 430–508 (2008–2012).
Conclusion: As cigarette smoking has decreased in Norway, the use of snus has increased correspondingly. The reason for this is possibly that there is a massive focus on health hazards with smoking in Norway whereas snus has been largely ignored. This is reflected in the increase in consumption of snus, especially amongst teenagers and young adults as a trend particularly over the last few years. We believe that these statistics probably give us the answer to the changes in inquiries to the poisons information center. The pattern of use is actually reflected in the poisons center telephone statistics. The availability of snus for children increases as the pattern of use changes from cigarettes to snus. Other reasons that might explain the drop in "cigarette" calls could be better information on our websites and larger focus on cigarettes on the whole, and parents' awareness. The availability of snus and also the presentation of snus render it more tempting for the young to taste than cigarettes.

101. Calls concerning electronic cigarettes to the Finnish Poison Information Centre

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Objective: Electronic cigarettes (EC) are battery-operated products designed to deliver nicotine, flavor and other chemicals. They turn all these into a vapor when inhaled. ECs are filled before inhaling with few drops of a flavored liquid from a small bottle (10–30 mL) containing various amounts of nicotine (0–40 mg/mL). Flavors range from bubble-gum to tobacco.
Methods: Retrospective review of the Finnish Poison Information Centre's (FPIC) call-records. During 1 January 2010–31 October 2013 FPIC received 74 inquiries concerning EC. General inquiries (10) and calls related to animal exposures (4) were excluded. The 60 remaining calls related to EC liquid were: spatter in the eye (9/60) or on skin (5/60), accidental or intentional ingestion (37/60), and inhalation exposures (9/59).
Results: The first call concerning EC was received in November 2010 (the only one that year). In 2011 there were 8 inquiries, 33 in 2012 and by the end of October 2013 there were already 33 inquiries concerning EC, while the number of calls to FPIC has remained unchanged; 53/60 of the cases were accidental, 5 were deliberate, and in 2 intentionality was unknown; 16/60 patients were aged under 6 years, 4 were 6–15 years of age and there were 31 adults ($\geq$16 years). Two calls concerned more than one patient and in 7 cases age was unknown. In 31/60 of the calls, the patient was symptomatic; symptoms were generally mild. In ingestion or inhalation exposures the main symptoms were nausea and/or vomiting. Exposures in the eye or on the skin caused irritation. In 18/60 the cases were instructed to stay at home, 28/60 were advised to seek medical attention if needed. 14/60 were referred to a hospital mainly for activated charcoal or the patient was already in hospital.
Conclusion. EC inquiries were less than 10% of all tobacco/nicotine related inquiries. In EC inquiries the patients were mainly young adults, while in tobacco/nicotine related inquiries the great majority were children under 6 years of age. The different age distribution of the calls related to EC may reflect the novelty and limited use of the products, although the picture may be changing rapidly. The liquid used in ECs seems to be mainly irritating.

102. E-cigarettes: A need for better quality regulation?

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Introduction: Electronic (e) cigarettes are supposed to be an aid to smoking cessation and therefore increasingly popular. The e-cigarette is a battery-powered, pen shaped, device which vaporizes the e-liquid into an aerosol mist which simulates tobacco smoking. The e-liquid contains propylene glycol with up to 36 mg/mL nicotine. E-liquid cartridges need to be refilled. The household presence of e-liquids containing high concentrations of nicotine creates a risk of accidental and intentional ingestions.
Methods: Retrospectively, from January 2007–November 2013, all cases of ingestion of e-liquids in the Dutch Poisons Information Center (DPIC) database were evaluated with regard to age, exposure circumstances, and health effects.
Results: 20 cases, 16 accidental and 4 intentional exposures, were identified; 2 in 2008, 1 in 2012 and 17 in 2013. Ten exposed persons were 18 years or older, four were between 13 and 18 years and six were 2 years or younger. The estimated ingestion ranged from 0.1 to 4 mg/kg bodyweight. However, due to lack of information about the specific product and ingested amount, the nicotine dose was uncertain in most cases. In at least four cases exposure was caused by leaking or broken e-cigarettes. The health effects reported were a burning throat (4), vomiting (5), nausea (3), dizziness (3), headache (2) and palpitations (1). Four children were admitted to hospital.
Discussion: The sharp rise in the number of calls to the DPIC in 2013 most likely reflects the increased use of e-cigarettes. E-cigarettes and e-liquids are widely available, also through the Internet, and unfortunately sometimes of inferior quality. Advertising campaigns promote e-smoking as a healthier alternative to regular cigarette smoking. In the Netherlands and other European countries opinions differ whether or not e-cigarettes should be regulated as medicines to ensure quality and safety. In 2012 the Dutch court decided to consider the e-cigarette as a non-medical product.
Conclusion: These poisons center data show the undesirable effects of the use of e-cigarettes, and justify the call for quality regulation of these products. As these products now have a non-medical status, this would mean involvement of the Food and Consumer Product Safety Authority.

103. Trends in electronic cigarette exposures reported to the National Poison Center database

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Objective: The Centers for Disease Control and Prevention (CDC) has reported an increase in electronic cigarette use in both adults and adolescents.[1,2] The American Association of Poison Control Centers specifically designated codes for these products in 2010, and to date, only limited studies using single poison center or regional data have described trends in these exposures. This study aims to characterize epidemiological trends in electronic cigarette exposures reported to the National Poison Center Database (NPDS).
Methods: NPDS data were queried for all calls to United States (US) poison centers from 1 June 2010 through 30 September 2013 for human exposures to electronic cigarettes. Demographic, exposure, and clinical characteristics were assessed. Changes in rates of call volume per month were analyzed using linear spline regression modeling
Results: A total of 1700 human exposures were reported to NPDS, of which the most frequent age groups were children ≤ 5 years (42.2%) and adults ages 20–39 years (27.4%). There were slightly more exposures reported among males (52.5%) than females (47.5%). The majority (84%) of patients had no more than minor effects reported/expected; one suicide was reported as a result of a single substance exposure. The greatest volume of exposures was reported in the western region of the US (26%), while the lowest volume was reported from the northeast (13%). Temporal trends showed an increase of 1.5 exposures per month [95% CI: 1.3–1.7] from June 2010 through January 2013, after which exposures increased by 10.6 per month [95% CI: 9.4–11.9] from February through September 2013. The change in rate in recent months was greatest in children ≤ 5 years, from 0.63 increased exposures per month [95% CI: 0.5–0.8] to 6.8 increased exposures per month [95% CI: 5.9–7.7].
Conclusion: This is the first study to use national-level poison center data from the US to characterize epidemiologic trends in electronic cigarette exposures. The volume of exposures is greatest for children ≤ 5 and 20–39-year olds. While the recent six-fold increase in reported exposures may be due to more diligence in coding practices, this trend may reflect changes in overall prevalence and availability of electronic cigarettes in households.

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104. E-cigarette liquid refills – a safe beverage? Analysis of enquiries to the UK National Poisons Information Service from 2007 to 2013

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Objective: To analyse calls to the UK National Poisons Information Service (NPIS) involving ingestions of e-cigarette refill solutions and to examine any recorded adverse effects.

Methods: Calls to the UK NPIS were analysed for enquiries relating to unintentional and intentional e-cigarette liquid ingestions between April 2007 and August 2013.
Results: The UK NPIS received a total of 150 enquiries, specifically concerning e-cigarette refill liquid ingestions. The data shows a significant increase in the number of telephone enquiries, rising from six calls in 2007 to over 75 enquiries from January to August 2013. The number of enquiries involving children aged 4 years and younger accounted for 36.5%, of which 10% developed features and required further hospital management. Adults accounted for 56.1% of these enquiries. A total of 14 cases (9.5%) displayed features of toxicity at more than 4 h post-ingestion. The most common features reported (at the time of the enquiry) were vomiting (11.9%), nausea (6.6%), dizziness (5.9%), and abdominal pain (3.9%). Features such as tachycardia, tremor, chest pain, dyspnoea, anxiety, and agitation were also recorded. Two cases involved significant and prolonged toxicity: a 20-year-old female ingested 1.5 mL of e-cigarette liquid. She developed vomiting, hematemesis, and melaena which persisted for 3 days post-ingestion. A 39-year-old male ingested an unknown quantity of e-cigarette liquid as a means of self-harm. Features included vomiting, confusion, bradypnoea, hypertension, tachycardia, and atrial fibrillation.
Conclusion: These liquid refills contain varying concentrations of nicotine. Other harmful, undisclosed ingredients including diethylene glycol and carcinogenic tobacco specific N-nitrosamines have also been detected in the solutions.[1] Results of this analysis indicate that these products have the potential to cause serious harm. Further regulation is essential in order to inform the public of the potentially serious effects of these readily available agents.

Reference

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105. School-based health promotion for poisoning prevention education in children: A National Poisons Information Service proposal to reduce poisonings in the UK

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Objective: To analyse calls to UK National Poisons Information Service (NPIS) and develop a school-based, poisoning prevention program aimed at pupils 4–11 years.
Methods: The UK Poisons Information Database (UKPID) was searched for poisoning enquiries between January 2008 and December 2012 for all cases involving children aged 0–11 years.
Results: The NPIS received a total of 84,967 calls regarding children up to and including 11 years of age during this period. Of these, 19.5% (n = 16 542) involved enquiries concerning the specific target group (4–11-year-old). The number of enquiries decreases with age, the highest proportion of the target group, (4–11 years) related to the youngest children, aged 4 years (33%). Not surprisingly, the most common location for poisoning incidence was the home (87.7%), followed by schools (6.4%), public areas (2.9%), hospitals (1%), and GP surgeries (0.4%). Accidental exposures accounted for 75% (n = 605) of these enquiries and 19.6% (n = 156) were recorded as therapeutic errors; 6.2% (n = 64) of enquiries were intentional exposures in those aged 9–11 years.
Conclusion: These data suggest that poisoning prevention educational programs, focusing on children between 4 and 11 years, may help to reduce the number of children exposed to potentially toxic agents. Previous educational programs have included stand alone, generalized sessions, however, it has been suggested that this method has resulted in a lack of retained knowledge.[1] Our proposed intervention aims to integrate poisoning awareness within the school curriculum by developing an age specific, hands-on topical approach. Schools could use these sessions as a starting point for further projects such as focused safety awareness weeks, whereby knowledge is more likely to be retained by pupils This intervention program, also anticipates that younger siblings will be inadvertently educated by their older brothers and sisters, an outcome reported with other prevention studies.[2]

References

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2. Butts JD, Beck CL. Education of young children concerning poison prevention. Public Health Rep 1986; 101:90–93.

106. Serious adverse events associated with liquid laundry pods exposure: A retrospective study by the French poison control and toxicovigilance centers from 2005 to 2012

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Objective: Over the past few years, exposure to liquid laundry pods has been responsible for severe pediatric poisoning. According to the Association for Soaps, Detergents and Maintenance Products (AISE), the number of pods sold in France increased from 300 to 700 million between 2010 and 2012. The French toxicovigilance network aimed to describe the recorded cases in a large time series, focusing on severe cases.
Methods: A retrospective study was carried out on cases of exposure to pods recorded from 2005 to 2012. Any person exposed to a pod, with or without symptoms, was defined as a case. The severity of cases was defined according to the affected organ and symptoms: eye (keratitis, corrosive lesions, corneal perforation), lung (respiratory distress, laryngospasm, aspiration pneumonia),

oral and digestive tract (oropharyngeal or oesogastric corrosive lesions, grade 2 or more). Severe cases without causality to pods were excluded.

Results: From 2005 to 2012, 7562 cases of exposure, with a significant increase since 2009 had been recorded. The sex ratio M/F was 1.1. The main cases were children aged 5 or less (92%); among them, 7% were aged less than 1 year. Route of exposure was oral (82%), ocular (17%), cutaneous (9%) and respiratory (0.5%). Symptomatic cases account for 67% of all cases, 87% among children aged 5 or less. The following symptoms were described: gastrointestinal (48%), ocular (13%), respiratory (12%) and cutaneous (3%). Drowsiness, confusion or hypotonia were found in 0.4% of cases, possibly due to a significant amount of glycols. In our study, 2% (n = 104) symptomatic cases were serious, including keratitis (n = 65), and respiratory distress (n = 6, including 3 acute respiratory distress syndrome (ARDS)). Complications persisted in 5 cases (1 amniotic transplant and 4 skin necrosis excisions).

Conclusion: Our study confirms the need to improve the safety of these very popular products and to inform the public of their specific hazards. More than 2% of cases were serious. Liquids (water or saliva) rapidly dissolve the hydrosoluble packaging and release highly concentrated contents, often under pressure. Further studies would be necessary to assess and follow-up the occurrence of cases and circumstances of exposure regarding the market's expansion of pods.

107. An analysis of the UK National Poisons Information Service consultant referral process

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Background: UK National Poisons Information Service (NPIS) clinical toxicologists (CTs) received 1540 referrals from specialists in poisons information (SPIs) in 2011/12. This study was performed to explore the views and experiences of the enquiry referral process for NPIS SPIs and CTs, to create awareness of the challenges faced by both parties and to explore ways of facilitating a more efficient referral process.

Methods: Anonymous, online questionnaires were used to collect the views of CTs and SPIs. Likert response scale questions were combined with a free text comments box. Responses were analysed to identify strengths and weaknesses of the current referral process, opportunities for improvement and potential barriers to change. Results were subsequently discussed with stakeholders.

Results: 42 of 43 SPIs and all 15 CTs responded (response rate 98%). Most responses indicated satisfaction with the process. Forty-seven per cent of CTs reported delays when contacting SPIs (partly due to telephone system problems), 40% that too few calls were referred (but none that too many referrals were made) and 20% that the information provided by SPIs is "only occasionally sufficient" for a clinical judgment to be made. Twenty per cent felt that SPIs relay information too quickly (but none felt delivery was too slow). Several CTs preferred to be told the reason for the referral at the start of the call, before a detailed clinical history is provided (13% in free text comments and 40% in subsequent discussion). A typical CT comment was "referrals are generally of a high quality." For SPIs, 10% reported problems in contacting the CT, 98% responded that the CT "usually" or "always" understands the reason for the call and 21% that CTs should always offer to speak to the enquirer directly. SPIs praised consultants who email a summary of the advice that they have given, as they value the support from CTs in documenting complex calls. Use of a standardized handover tool for information delivery was supported by 53% of CTs and 52% of SPIs.

Conclusion: Whilst most responses indicated satisfaction with the process, this survey has highlighted areas for improvement, many of which can be achieved by enhanced awareness and training for both groups.

108. Toxicity of reed diffusers: A retrospective analysis of telephone enquiries to the UK National Poisons Information Service 2010–2012

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Objective: To ascertain the reported toxicity of reed diffusers. Reed diffusers are vessels filled with fragranced liquid, "wicking" reeds and, sometimes, water beads. Their composition varies and includes essential oils, glycol ethers, isopropanol, petroleum distillates and ethanol.

Methods: We analysed retrospectively UK National Poisons Information Service (NPIS) enquiry data collected between 1 January 2010 and 31 December 2012.

Results: 324 UK patients were exposed to reed diffusers; the majority (n = 305) were children < 5 years. The identity of the reed diffuser was known in 221 cases (68.2%); most (n = 152) exposures were from the Airwick™ range, which contain propylene glycol monobutyl ether, petroleum distillates, essential oils, and fragrances. Ingestion alone was the most common route of exposure (305 of 324 patients) and involved the liquid alone (n = 247), the water beads alone (n = 36), the liquid and water beads (n = 11) or sucking on the reed (n = 11). The WHO/IPCS/EC/EAPCCT Poisoning Severity Score (PSS)[1] was known in 304 ingestions: in 246 (80.9%) the PSS was 0 (asymptomatic); in 52 (17.1%) patients the PSS was 1 (minor toxicity); in 6 (2.0%) the PSS was 2 (moderate toxicity); there were no patients with PSS 3. Features included nausea and vomiting (n = 32); abdominal pain (n = 1); diarrhea (n = 1); decreased appetite (n = 1); coughing (n = 7); gagging (n = 3); lip swelling, redness or irritation (n = 3); facial oedema (n = 1); bad taste (n = 1); sore mouth (n = 2); tongue blistering (n = 1); dysphonia (n = 2); epiglottic swelling (n = 1); stridor (n = 1); bronchospasm (n = 2); hypoxia (n = 2); central nervous system depression/drowsiness (n = 4), one of whom suffered respiratory depression; sinus tachycardia (n = 2); ectopic beats (n = 1); tremor (n = 1); tonic-clonic convul-

sion (n = 1); pallor (n = 2) and fever (n = 1). Dermal exposure alone was reported in four patients, only one of whom was symptomatic with skin irritation. Three patients suffered eye exposure and complained of eye pain (n = 2) and conjunctivitis with irritation (n = 1). Multiple routes of exposure occurred in twelve patients: six were asymptomatic; in five the PSS was one and in one was unknown.
Conclusion: Although reed diffusers have a high potential to cause serious toxicity, the majority of patients in our study developed no or only minor symptoms, probably because most exposures involved the ingestion of only small quantities of fragranced liquid.

Reference

1. Persson H, Sjöberg G, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol 1998; 36:205–213.

109. Consequences of the inappropriate use of professional grade pesticides: An analysis using National Poisons Information Service Pesticide Surveillance Survey data

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Objective: Professional grade pesticides are more hazardous than their consumer grade counterparts and should only be used occupationally. It is legally required that those who use professional pesticides receive training/certification and use protective equipment. National Poisons Information Service (NPIS) surveillance has historically indicated a high incidence of non-occupational use of professional pesticides. Our objective was to evaluate the repercussions of such inappropriate use.
Method: The NPIS has monitored pesticide exposures as part of a pesticide surveillance study since April 2004. Data is collected by monitoring NPIS unit calls and TOXBASE® accesses. The WHO/IPCS/EC/EAPCCT poisoning severity scores (PSS)[1] for exposures relating to both occupational and non-occupational use of professional products were analysed.
Results: Between April 2004 and April 2013, information on 7052 unintentional pesticide exposures was collected; 1312 were due to professional products. Of these exposures, 643 (49%) were reported as occurring during non-occupational use, 556 (42.4%) during occupational use, and in 113 cases circumstances were unknown. The severity grading for these exposures is shown in Table 1. Most non-occupational exposures elicited none or few features. Significantly more occupational exposures resulted in the development of PSS 1/2 ($X^2 = 128.889$, d.f. = 1, $p < 0.05$). Severe or fatal cases were uncommon for both exposure types.
Conclusion: Occupational exposure to professional grade pesticides was more likely to result in the development of features of poisoning; usually of minor or moderate severity.

Table 1. Severity of non-occupational and occupational exposures.

Severity	Non-occupational (n = 643)	Occupational (n = 556)
PSS 0 (None)	322	99
PSS 1 (Minor)	251	330
PSS 2 (Moderate)	42	80
PSS 3 (Severe)	7	7
Fatal	1	2
Uncertain	20	38

Reference

1. Persson H, Sjöberg G, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol 1998; 36:205–213.

110. National Poisons Information Service urgent alerting system for chemicals: Data from the first year

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Objective: The UK National Poisons Information Service (NPIS) has established a real-time reporting system with healthcare professionals in the UK, whereby accesses to 143 entries of interest on TOXBASE®, the UK's primary poisons database, generate an urgent e-mail alert to NPIS units within 10 min. The alert gives user details, location, time, and whether a specific patient is involved. NPIS contacts the user, and enters details of follow-ups into the UK poisons information database (UKPID), with a tag. We now report the first full year of data generated by this system.
Methods: All tagged call records for one year from 1 April 2012 to 31 March 2013 were extracted from UKPID for analysis.
Results: During the study year, 127 of the 143 selected chemical pages were accessed 10,892 times by 962 different users. Of these, 2636 alerts (24.2%) were marked as involving a patient and user contact details entered for 424 (16.1%). Excluding overseas accesses, multiple accesses and cases already known to the NPIS, 289 alerts were followed up, and further details collected from 252 cases. An additional 13 follow-ups were made where there had been multiple accesses but no user details were entered. Of the 265 cases, 202 (76.2%) related to 1 patient and 40 (15.1%) related to a population (median 3 patients, range 2–22). Exposures were most frequently accidental (n = 198, 74.7%), by inhalation (153, 57.7%), and occurred at home (112, 42.3%), and were managed in hospital (248, 93.6%). The most common agents involved were carbon monoxide (93, 35.1%), chlorine (33, 12.5%), and ammonia (13, 4.9%). An NPIS consultant was involved in 26 (9.8%) follow-ups. The maximum WHO/IPCS/EC/EAPCCT Poisoning Severity Score (PSS)[1] was recorded in 205 cases: this was 0 in 46 (22.4%), 1 in 129 (62.9%), 2 in 20 (9.8%), and 3 in 10 cases (4.9%). There were 15 calls alerted to Public Health England Chemicals and Poisons Division.

Conclusion: This mechanism allows detection and rapid response by NPIS to cases of poisoning involving highly toxic agents across the UK, facilitating rapid provision of information including consultant advice, and prompt alerting of public health bodies to potentially serious chemical incidents.

Reference

1. Persson H, Sjöberg G, Haines JA, et al. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol 1998; 36:205–213.

111. Added value of poisons centers in the response to radiological incidents

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Objective: The Fukushima nuclear power plant disaster (Japan, 2011) and increased terrorist threats during the last decade have raised awareness for incidents involving radioactive material. Poisons centers (PC) can play an important role in the preparation for, and immediate medical response to, radiological incidents.
Methods: In the Netherlands, the PC is officially embedded in the response network for radiological incidents. Radiation protection experts are available 24/7. Knowledge on radiotoxicity is essential to calculate radiation dose and perform risk assessment after radionuclide exposure. The tasks PCs can perform are illustrated by recent involvement in exposure assessment and incident preparedness.
Results: In 2013 the Dutch PC was consulted about several suspected radionuclide exposure cases. Hematologists asked the PC's radiation experts to assess the relationship between unexplained aplastic anaemia and chronic exposure to dust from uranium-containing minerals. Calculation of possible bone marrow dose made such a relationship unlikely. Another consultation concerned a patient with gastrointestinal complaints, hematuria and epistaxis after supposed iridium exposure. Thorough questioning revealed no radiological exposure. The PC plays an important role in advising the authorities and healthcare professionals on radiological incident management for cases with ionizing radiation in or outside the Netherlands in which Dutch citizens might be involved. After internal contamination with radionuclides, elimination can often be enhanced by administering antidotes. On PC recommendation, the Ministry of Health erected a stockpile of the chelators diethylenetriaminepentaacetate (DTPA, for e.g., plutonium, americium and other actinides) and Prussian Blue (for cesium and thallium). Thereafter healthcare professionals and policy officers were trained on radiotoxicity and medical management. Recently, a near incident with a nuclear facility with the possibility of exposure to several radionuclides led to the installation of an incident response team. The PC experts were part of this team and informed about possible health effects.
Conclusion: In the last year the Dutch PC radiation experts have assessed individual radiological exposures, have trained healthcare professionals on radiotoxicity and have acted as experts in radiological incident response teams. In this way the radiological expertise of the PC showed its added value to health care personnel and the Dutch authorities.

112. National register of acute poisonings: Role of the poison information center

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Objective: The poisons information center (PIC) at the Clinic of Toxicology started registering poisonings in the whole country in order to follow poisoning trends and characteristics and take preventive measures.
Method: A questionnaire is attached to the web site of the PIC. According to the Chemicals Law in Macedonia, each Medical Center and Clinic outside the PIC has to report all diagnosed and treated poisonings by completing and sending the form to the Center.
Results: There were 1301 acute poisonings registered in 2012 in our country or 9.2% more than 2011; 11.4% were poisonings in children under 14 years of age. The greatest number of poisonings was in September (11.5%) and May (10.4%). 4.2% of the poisonings were suicidal which was significantly less compared to 2011 (53.3%). In 2012 as in 2011, medication poisonings were most frequent (43.7%), mainly benzodiazepines (50%), and there was only one poisoning with paracetamol. In contrast to 2011 when chemical poisonings were second (21.4%), in 2012 poisonings with ethyl alcohol were more represented (27.2%). The most common chemical poisonings were corrosive (50.1%), representing 10.4% of the total number of poisonings and less than in the year 2011 (15.2%). Hydrochloric acid was the most used substance (50% of all the corrosives) and opioid overdoses were registered in 5.2% of the poisonings which was a slight increase compared to 2011 (4.6%). In children under 14 years, medication poisonings were most common (63.7%), mostly with benzodiazepines (32%). Chemical poisonings dropped to 27.4% compared to the year 2011 (48.8%). Corrosive poisonings also decreased in 2012 (38%) compared to 2011 (51%). One case of severe poisoning with ethyl alcohol and one case of a heroin overdose were registered in this population group in 2012.
Conclusion: The increase in alcohol poisonings and opioid overdoses shows that the social movements in our country are following the patterns of other European countries. The decreases in chemical poisonings in adults and in children are the result of better awareness of their toxicity and the taking of safety measures.

113. Sympathomimetic toxicity caused by adulterated food supplements for weight loss

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Background: Food supplements are widely available over the counter as well as through the Internet. Food supplements often contain substances that are not mentioned on the label and that may cause health damage. In 2013 the Dutch Poisons Information Center (DPIC) raised an alarm regarding two different weight loss and sports enhancement products ("Iomax®" and "Dexaprine®"), both inducing significant toxicity after use according to the product label.
Case series: Iomax®: Up to October 2013 the DPIC received 13 inquiries regarding Iomax®, a product sold via cell phone contacts on Internet message boards. Even when using only half a capsule, patients reported symptoms shortly (hours) after they started taking the product. These symptoms included palpitations, anxiety, tachycardia, and chest pain. Several patients were admitted to an intensive care unit. The DPIC informed the Netherlands Food and Consumer Product Safety Authority (NVWA) and they posted a warning for users on their website. Analysis of Iomax® capsules performed by the National Institute for Public Health and the Environment (RIVM) revealed 100–120 mg of amphetamines. Dexaprine®: In the first 8 months of 2013, the DPIC received 22 calls regarding another slimming product, Dexaprine®, sold via several Dutch web shops. The patients experienced gastrointestinal symptoms as well as palpitations, tachycardia and agitation after using the product as indicated on the label. In August 2013, the NVWA received information about a woman having a cardiac arrest after the use of Dexaprine®. After information exchange between NVWA and DPIC, a warning was posted on the site of the NVWA and in the national media. Web shops were ordered to recall the product and to send a letter to previous buyers informing them about the possible risks. Preliminary testing results (RIVM) of these tablets show methamphetamine as one of the components.
Conclusion: Poisons centers can contribute to recognition of unsafe food supplements through registration and monitoring of product information and health effects reported after intake. Good cooperation between poisons centers, laboratories, and enforcement authorities is important for the rapid identification and quantification of substances, the subsequent risk estimation, and management.

114. Use of Cloud technology reporting systems to motivate and improve staff performance in a poisons information service setting

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Background: In Spring 2012 the UK National Poisons Information Service (NPIS) started using Cloud technology, BT Cloud Contact™, to provide its staff and service users with a robust, integrated telephone service from its four units. Similar systems are used worldwide for call-center type operations. The standard reporting capabilities of such systems provide supervisors with detailed analysis of operator activity at an individual level.
Objective: To investigate whether providing the specialists in poisons information (SPIs) at the NPIS (Birmingham Unit) with their personal data improved performance.
Methods: Detailed statistical data on SPI performance were extracted from the Cloud interface. Reports were provided to staff monthly from November 2012 to October 2013 following review by the management team.
Results: From February 2013, staffing nationally was increased from 2 to 3 SPIs between 6 pm and 10 pm on weekdays, and 2 pm and 10 pm at weekends. After the change the mean waiting time (± SD) for quarter 3 (June–August) was 16 (± 4)s, and for quarter 4 (September–November) was 17 (± 4)s, which were significantly lower ($p < 0.002$) than the mean waiting time (± SD) for quarter 2 (February–April) of 36 (± 10)s. For the hours outside these periods, where staffing remained constant, the mean waiting time (± SD) for quarter 2 was 40 (± 7)s, for quarter 3 was 18 (±3) s, and for quarter 4 was 16 (± 4)s, which were all significantly lower ($p < 0.001$) than the mean waiting time (± SD) for quarter 1 of 54 (± 14)s. There was no significant difference ($p \geq 0.05$) for the other parameters: mean enquiry duration, percentages of phone time handling enquiries, documenting enquiries, time on breaks and time available for other duties.
Conclusion: Distribution of personal data was effective in reducing call waiting times but not other parameters of performance. Time spent handling and documenting enquiries remained constant indicating that having calls queuing did not impact. Key performance indicators, based on these findings, will now be set for SPIs to measure their performance against.

115. Agreement on product information requirements for Poisons Centers in European Union Member States

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Objective: Based on article 45(4) of the CLP Regulation (EC) No 1272/2008, the European Commission seeks to harmonize product notification by companies to Poisons Centers and Competent Authorities in European Union (EU) Member States. An important step towards harmonization was finding consensus with stakeholders on product information requirements, especially on the degree of composition detail.
Method: The EAPCCT Working Group on Poisons Centers Activities/European Regulatory Issues defined product information requirements in 2010. Discussions of EAPCCT representatives with industry associations, Competent Authorities and the European Commission resulted in modification of the requirements[1] that are included in the amended "EAPCCT Guidelines 2013" and were endorsed by the EAPCCT Board.
Results: Stakeholders have agreed to use flexible concentration ranges for ingredients, as an alternative to exact concentrations. Maximum allowed range widths are based on the hazard classification and the actual concentration of the ingredient in the mixture.[1] In addition, it was agreed to use concentration thresholds. All ingredients classified as hazardous in a concentration above 0.1% have to be notified. Below 0.1% only identified hazardous substances have to be notified (which excludes the notification of

possible additives or impurities being part of a substance). All non-classified ingredients above 1.0% have to be notified. Below the threshold the identified ingredients are qualitatively notified. Furthermore, industry requested reduced notification requirements for mixtures for industrial use. The substantial notification workload is seen as disproportional to the relatively low number of industrial exposures Poisons Centers have to deal with. As a compromise, the Safety Data Sheet is accepted, provided that detailed composition information is rapidly available 24 h/7 days. A study to evaluate the workability of this solution will be conducted.
Conclusion: The European Commission will present the information requirements at the November 2013 Meeting of Member States Competent Authorities on REACH and CLP (CARACAL). If endorsed, the European Commission will develop a legislative proposal to add an Annex to the CLP Regulation describing EU harmonized product information requirements.

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116. The impact of changes to packaging and labelling on exposures to liquid laundry detergent gel capsules

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Objective: During 2013 the manufacturers of liquid laundry detergent gel capsules (gel capsules), introduced voluntary changes to the packaging and labelling of these products, with the aim of reducing the number of cases of accidental poisoning. This study was performed to characterize enquiries to the National Poisons Information Centre of Ireland (NPIC) about exposures to gel capsules, and to assess the impact of these changes.
Methods: Enquiries to the NPIC between 1 January 2012 and 31 December 2012 about exposure to gel capsules were retrospectively identified on the enquiries database and data were extracted on month of exposure, patient demographics, route of exposure, symptoms, and Poisoning Severity Score. The same data were collected prospectively on cases exposed between 1 January and 30 September 2013.
Results: A total of 370 patients were exposed to gel capsules: 220 in 2012 and 150 during the first 9 months of 2013. Ingestion was the most common route of exposure (299 cases, 80.8%), 34 (9.2%) patients were exposed by eye contact and 21 patients by ingestion plus eye contact (5.7%). The majority of patients were children less than 5 years old (339 cases, 91.6%) and 187 (50.5%) were $\leq$1-year old. Two hundred and forty-three (66.3%) cases were symptomatic: 227 of these patients had minor symptoms and 16 had moderate symptoms. There were 150 cases of gel capsule exposure from January to September 2013 compared to 182 during the same period in 2012, an overall reduction of 17.6%. However, this reduction occurred during the first 6 months of 2013 only. Cases rose again during July–September 2013 and were 10.5% higher than in 2012.
Conclusion: Most patients exposed to gel capsules were children less than 5 years old, who had ingested the product. A high proportion of cases (66.3%) were symptomatic, although most (94.3%) had only mild symptoms. An initial reduction in cases during the first 6 months of 2013 was not sustained during the third quarter, despite greater availability of products in opaque/obscure packaging.

117. Supporting the Union level co-ordinated assessment and management of cross border chemical health threats

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Objectives: Historically the public health response to chemical events that affect more than one country has been varied. With the adoption new European Union (EU) legislation co-ordination of the public health response at the Union level has been agreed. Poisons Centers and Public Health Authorities will play a significant role in the identification, alerting and notification of potential health threats involving chemical exposures to populations. This paper explores the implications of the adoption of the Decision (1082/2013/EU) on Serious Cross Border Threats to Health and relevance to EU Poisons Centres.
Methods: Two complementary collaborative research projects on transboundary chemical health threats were co-funded by the EU Commission under the 2008–2013 Health Programme. These projects termed Alerting, Reporting and Surveillance Systems for Chemical Health Threats (ASHTIII) and the establishment of a European Chemical Emergency Network (ECHEMNET) focus on the following areas: Networks of experts to aid in the acute phase response at the Union level; Rapid Risk Assessment Methodologies for cross border incidents; Tools and approaches to support ad-hoc surveillance; Guidance on inter-sectoral alerting and reporting; Chemical Emergency Risk Management Monographs
Results: Progress has been made in each of the areas indicated above for both ASHTIII (year 2) and ECHEMNET (year 1) and work is ongoing. Both projects require significant engagement and feedback from EU Poisons Centres to ensure that the toxicological aspects of the deliverables are robust. The final project deliverables will contain recommendations to the Commission regarding the approaches and tools developed to aid implementation of the Decision.

Conclusion: Work is on-going via two inter-related EU co-funded projects to aid the implementation of the Decision for Serious Cross Border Threats to Health. Here we present the work-to-date and describe how the project deliverables could be applied to support the Union, Member State and Poisons Centre response to transboundary chemical health threats.

118. Survey of toxicological analyses availability in the Italian National Health System: Preliminary results and a national pilot database

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Objective: To survey the availability of toxicological laboratories and analyses in the Italian National Health System, with special reference to the medical emergency setting; to improve the use of toxicological analyses for the appropriate diagnosis of poisoned patients; to facilitate the identification of analytical services and performed analyses all over Italy for the clinical management of poisoned patients, mostly through the creation of a "National Toxicological Analyses Database".
Methods: In April 2012 a questionnaire was made available online and sent by post to the laboratories of all Italian hospitals, requiring information on the availability of more than 500 molecules that can be the cause of poisonings and that are relevant for the diagnostic process. Several categories of potentially toxic agents have been investigated, with reference to chemicals (conventional and non-conventional agents), drugs, drugs of abuse, pesticides and natural toxins.
Results: Completed questionnaires were received from 190 hospitals' laboratories; for every molecule, data on analytical methods, specimens, turnaround times and emergency availability were provided by participants. Preliminary data on all the Italian regions have been analysed. Among drugs, serum paracetamol analysis results were available in 22 laboratories (15 of them on 24 h basis), whereas digoxin in 141 (108 on 24 h basis). Among chemicals, methanol determination is available in 6 laboratories (1 on 24 h basis), serum ethylene-glycol in 2 (1 on 24 h basis). Among drugs of abuse, urinary and blood ketamine analysis is available in 4 laboratories (not on 24 h basis), methadone in 100 (75 on 24 h basis), buprenorphine in 41 (15 on 24 h basis).
Conclusion: This survey allowed us to become aware of toxicological resources in the analytical field all over Italy, to georeference the laboratory and analysis availability, to identify areas for improvement and, possibly, to ameliorate the availability of toxicological tests for clinical departments, optimizing resources. The "National Toxicological Analyses Database" is the tool that allows the rapid identification of the available resources.

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119. Development of syndromic surveillance system in toxicovigilance: Lessons learned from mushroom poisonings and Hymenoptera envenomations in France

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Objective: In France, toxicological inquiries from citizens and health professionals and human poisoning cases are collected by poison control centers (PCC) through a national information system. This study aimed to assess the feasibility of using syndromic surveillance data from emergency departments to complete the PCC specific surveillance system.
Methods: The French Institute for Public Health Surveillance (InVS) has developed a syndromic surveillance system (OSCOUR®) which collects daily and automatically epidemiological data for patients consulting in the 414 participating emergency departments (coverage rate higher than 65% in France). Two topics have so far been developed based on cases reported by the OSCOUR® and PCC systems: mushroom poisonings and Hymenoptera envenomations. As emergency departments and PCC data curves differed from normal distribution, the strength of a relationship between these data has been measured by Spearman correlation coefficient (r). Significance tests (p value) have been performed.
Results: Since 2010, surveillance of mushroom poisoning cases has been conducted. From 2010 to 2012, 1265 emergency consultations (OSCOUR®) and 4234 poisoning cases (PCC) were reported during seasonal monitoring periods (July-December). A very strong positive correlation has been identified between emergency departments and PCC data in seasonal time series ($r = 0.88$, $p < 0.01$). Due to the growing spread of the Asian hornet, InVS has undertaken a seasonal surveillance of Hymenoptera sting cases. From 2010 to 2012, a total of 22,747 emergency consultations and 1560 poisoning cases were reported during seasonal surveillance periods (April-October). Since 2010, seasonality trends of OSCOUR® data are consistent with those from the PCC specific surveillance system ($r = 0.90$, $p < 0.01$).
Conclusion: OSCOUR® is an emergency monitoring network with limited specificity, particularly in terms of exposure agent. However, these results suggest that it can be considered with a temporal perspective as an alert system, which allows the constitution of historical time series. Further investigations will be necessary to determine if the data collected from this source may contribute to the assessment of the burden of health events related to other toxic phenomena and describe their main epidemiological features. In toxicovigilance, multidisciplinary expertise and queries of different data sources are essential to assess unusual signals for public health.

120. The Global Educational Toxicology Uniting Project

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Objective: The Global Educational Toxicology Uniting Project (GETUP) is a not-for-profit project aimed at connecting countries with and without established clinical toxicology resources. International boundaries to medical education are becoming less marked as new technologies including multiuser-videoconferencing become more accessible. Videoconferencing allows real-time interaction between multiple geographically separate audiences. In 2013, the Austin Hospital Toxicology Service, Victoria, Australia; Fresno Toxicology Service, California, USA and Colonial War Memorial (CVM) Hospital, Suva, Fiji became the pilot sites for GETUP. The aims of the pilot were: 1. Connection of countries with and without clinical toxicology services through videoconference, enabling educational clinical toxicology case-based discussion. 2. Establishment of connections between health services around the world, facilitating improvement in clinical toxicology education.
Methods: The pilot study was conducted June-November 2013. Initial recruitment was via the Fiji site requesting remote help with toxicology education from the Austin site. Twelve subsequent sites were approached to be involved in GETUP via the American College of Medical Toxicology (ACMT) International Committee. Google Hangouts® was used as the videoconferencing software. Questions and cases were emailed before videoconference sessions and summarized learning points were circulated afterwards. Outcomes measured were perceived user feasibility, user satisfaction and rates of technical error
Results: Six videoconferences were conducted. A mean of five clinical cases were presented and discussed per conference. One hundred per cent of videoconference sites gave positive responses for feasibility and user satisfaction. Initial technical error rate was 1–2/conference; this rate subsequently fell to 0–1/conference. In addition to the 3 initial pilot sites, 15 different centers in 9 countries responded positively to a project invitation. Four were in developing and 5 in developed nations. Ten centers have access to toxicology fellowship programs and poisons information centers; one has limited access and four no access to clinical toxicology resources.
Conclusion: The GETUP pilot study demonstrated the technical feasibility of conducting worldwide multisite clinical toxicology case-based education. User feedback demonstrated high rates of satisfaction. Initial responses to invitations designed to extend the project have been positive. Videoconferencing may be an effective method of providing education to health care settings without extensive access to clinical toxicology resources.

121. Aluminum toxicity in infants & children: What's known and what isn't

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Introduction: Aluminum is a ubiquitous metal, present in many household utensils and products, cosmetics, water, vaccines, medicines, and foodstuffs. Consequently it is also found in human tissues; in one study of 25 healthy term infants, newborn plasma aluminum levels already averaged 9.9 μg/L.[1] Aluminum has no physiological role in humans and it has known toxicity.
Objectives: To address which children are most vulnerable to aluminum toxicity, to describe symptoms and physical findings in aluminum overload states, and to review research needs in the assessment of a child's aluminum body burden.
Discussion: Vaccines given at a single well child-care visit can contain up to 1200 μg of aluminum added as an adjuvant.[2] Human milk has between <5 and 65 μg/L of aluminum, while cow's milk-based formulas can contain 15–400 μg/L and soy-based formulas between 500–2400 μg/L.[3] A minimum risk level (MRL) for chronic aluminum intake was set by the U.S. governmental Agency for Toxic Substances & Disease Registry (ATSDR) in 2008 at <1.0 mg/kg/day.[4] Children only absorb 0.01–1.0% of ingested aluminum and can eliminate up to 85% of an aluminum load within a few weeks,[5] with the rest being distributed mostly via transferrin to tissues such as lung, kidneys, liver, and brain and then eliminated more slowly. Bone represents the principal long-term reservoir of aluminum accumulation. Premature infants receiving total parenteral nutrition, infants and children with chronic renal failure on hemodialysis or receiving phosphate-binders, and those with chronic gastrointestinal dysfunction receiving aluminum-containing antacids are among those groups at highest risk of elevated body aluminum burdens. Since aluminum is eliminated in urine, very premature infants with immature kidney function are also particularly vulnerable to aluminum loading. There is confusion in what is considered a normal pediatric aluminum concentration. Our group previously reported that commercial laboratories do not have uniform "norms" for either blood or urine for aluminum, e.g., blood normal ranges were variously set at <6 μg/L, <10 μg/L, <20 μg/L, or <40 μg/L.[6] Target organs for aluminum-related toxicity include the bones, neurological system, blood, liver, and parathyroid gland. Aluminum can cause an erythropoietin-resistant, microcytic anemia. Children with aluminum poisoning may suffer symptoms of encephalopathy including gait disturbances, myoclonus, abnormal electroencephalograms (EEG), depressed consciousness and/or seizures. Osteomalacia and spontaneous fractures reflect impaired parathyroid function, disturbances in calcium homeostasis, and bone toxicity. Neonates exposed to high daily parenteral doses of aluminum were found to have reduced lumbar spine and hip-bone mass 15 years later.[7] Deferoxamine, used as a chelation agent in patients with renal failure on dialysis who have progressive aluminum-related osteodystrophy, can reduce bone aluminum stores.[8] There has been speculation about the relation of low body burdens of aluminum and the origins of autistic spectrum disorders and other childhood neurological conditions. Further

research is needed in terms of the association between chronic aluminum loading and adverse behavioral, cognitive, learning or other developmental effects in children. In a preliminary study of aluminum levels in normal one-year olds (N = 41) and their development progress as measured by the Bayley Scales of Mental & Motor Development, our group found no significant associations between hair or whole blood aluminum levels and language, cognitive, motor, social-emotional, or adaptive domains.

Conclusion: While aluminum has known toxicity among certain groups of chronically ill infants and children, the effects of low body burdens and aluminum exposures at background doses in otherwise normal children are still unclear.

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122. Ciguatera outbreak in Germany in 2012

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Objective: Ciguatera is one of the most frequently recorded fish poisonings. It is caused by ciguatoxins, synthesized by dinoflagellates (e.g., *Gambierdiscus toxicus*) found on coral reefs. Dinoflagellates are ingested by eatable fish. Traditionally, ciguatera is observed in tropical and subtropical coastal regions, e.g., the Caribbean. Poisons centers (PC) in middle and northern Europe had only recorded rare cases of tourists returning from holiday. This is first report of a mass outbreak of ciguatera caused by fish purchased from supermarkets in Germany.

Methods: All cases of ciguatera reported to the PC were extracted from the PC case database, followed-up, and analysed.

Results: In November 2012, the PC was consulted 11 times due to poisoning after ingestion of Red Snapper (*Lutjanus malabaricus*), purchased from different shops of a single trade chain in six cities of northern and central Germany. In total, 11 patients that had eaten this fish on 7 November 2012 or a few days later developed poisoning symptoms: all patients were suffering from nausea, vomiting and diarrhea, in most cases starting about 4–6 h after the dish. Concomitantly paraesthesia of mouth, hands, and feet and dysfunctional temperature perception developed. The latter symptoms lasted – with decreasing intensity – for 3 weeks and in some cases longer. Furthermore, most patients complained of sleeping disorder, myalgia, and intense general weakness. Based on the very characteristic symptoms ciguatera was diagnosed early in most, but not in all cases. Analytical confirmation by a specialized laboratory in Spain was achieved 2 months after the outbreak. There is no specific treatment for ciguatera; all patients were treated symptomatically. Local food surveillance authorities, the trade chain and the importing company were informed early by the PC and the fish was withdrawn from the market rapidly. The product was delivered by a company from India, and thus fish was traced back to a tropical area.

Conclusion: To our knowledge, this was the first Ciguatera outbreak in Germany. This incident could be expected to reappear due to increased global food trading and, maybe, global warming. Alertness of poisons centers facilitated early detection and management avoiding more poisoning cases occurring.

123. Measurement of venom and clotting function in patients with Russell's viper coagulopathy and response to antivenom

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Objectives: Russell's viper envenoming is a major problem in South Asia and the major envenoming syndrome is venom induced consumption coagulopathy (VICC). The aim of this study was to investigate the kinetics of venom and dynamics of clotting function, including response to antivenom, in Russell's viper envenoming.

Methods: Russell's viper envenomings were included from a prospective cohort of snake bite patients in Sri Lanka. Age, sex, bite time, clinical effects, and treatment were recorded. Serial citrated plasma and serum samples were collected in all patients. International normalized ratio (INR), prothrombin time (PT), activated partial thromboplastin time (aPTT), coagulation factors I, II, V, VII, VIII, IX and X, were measured. Venom was measured in serum samples by enzyme immunoassay (EIA).

Results: There were 147 definite Russell's viper envenomings; median age, 39 years (16–82 years) and 111 (76%) were males. All patients had VICC and 70 (48%) had neurotoxicity. The median peak INR was 6.8 (interquartile range (IQR): 4–> 13) which was associated with low fibrinogen [median, < 0.2 g/L; IQR: < 0.2–1 g/L), low factor V levels [median < 5%; IQR: < 5–5.2%] and low factor VIII levels [median; 24%; IQR: 9–42%]. There were smaller decreases in factors II, IX and X. The INR, fibrinogen, factors V and VIII recovered over 48 h post-antivenom. Factor VII levels were initially very high post-bite, median maximum concentration, 300% (IQR: 100–645%),

and then rapidly decreased. The time course of factor VII directly correlated with venom concentrations, suggesting this may be *in vivo* activity of the venom. Venom concentrations remained detectable post-antivenom in many cases and there was apparent recurrence 40 h post-bite. In contrast to recurrence of venom concentration factor VII levels did not recur, suggesting neutralization of venom activity, and EIA measuring inactive bound venom.
Conclusion: Russell's viper VICC is characterized by low fibrinogen, low factors V and VIII, which recovered over 48 h. High factor VII activity before antivenom and its immediate decrease after antivenom, suggests it may be a good marker of venom activity.

124. Negative predictive value of excluding embedded snake foreign body by ultrasound

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Objective: Despite the low incidence of retained foreign bodies (FB) following a snake bite, numerous reputable sources for health care providers advocate routine imaging to rule out an embedded tooth or fang. The objective of this study is to determine if these foreign bodies can be reliably excluded by bedside ultrasound.
Methods: All Emergency Medicine (EM) residents and faculty at a single institution were invited to participate in this study. Two sets of five ultrasound gel phantoms were prepared using a method previously validated to have the same density as human tissue. In the first set of five phantoms, one snake fang was embedded to simulate a retained foreign body following a venomous snake bite. In the second set of five phantoms, one snake tooth was embedded to simulate a retained foreign body following a non-venomous snake bite. Participants were informed that the incidence of retained foreign bodies is low and were then asked to identify the presence or absence of a foreign body in each phantom using a Sonosite M Turbo® bedside ultrasound. Participants were shown an image of a fang and tooth as seen on ultrasound but no other training was given. Year of training and confidence in excluding a snake FB were also recorded.
Results: Each participant (n = 27) performed an ultrasound on 10 phantoms for a total of 270 samples. Range of experience included: PGY-1 (25.9%), PGY-2 (29.6%), PGY-3 (33.3%), and graduates of EM residency (11.1%). The sensitivity and negative predictive value (NPV) for ruling out an embedded snake fang was 92.6% and 98.1%, respectively. The sensitivity and NPV for ruling out an embedded snake tooth was 77.8% and 80%, respectively. Among all the phantoms there was a sensitivity of 85.2% and an NPV of 96%. There was no difference of accuracy by training year.
Conclusion: The overall NPV and venomous snake NPV was greater than 90%. Bedside ultrasound performed by an EM physician remains a viable option to rule out embedded foreign body following a snake bite and should be considered as an alternative to X-ray if imaging is deemed warranted.

125. Predicting the severity of common krait envenomation at presentation: What signs to trust?

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Objective: In this study, we evaluate ocular involvement at presentation and correlate it with severity of envenomation.
Methods: A prospective cohort study was conducted in the emergency department at our center. Patients presenting with neuroparalysis without local signs were included. Study period January to December, 2010. Data extracted included demographic details, the time and site of bite, symptoms and signs, need, type and duration of ventilation, duration of the hospital stay and final outcome. Clinical cranial nerve involvement was looked for. Patients were divide into three groups, Group A (isolated 3rd cranial nerve), Group B (3rd, 4th, and 6th cranial nerve), and Group C (3rd cranial nerve with other nerves except 4th and 6th nerve). Logistic regression and univariate analysis were used to predict the effect of various confounding factors on the outcome and duration of hospital stay. P value < 0.05 was considered statistically significant.
Results: 69 patients with neuroparalytic snake bite during the study period were enrolled. 78.3% victims were males. Mean age was 29 $\pm$ 3.5 years. The most common site of bite was upper limb (32%) followed by lower limb (29%). Five patients had no signs of envenomation. Twenty-six patients had isolated 3rd cranial nerve involvement (Group A) and thirty-one had complete ophthalmoplegia (Group B) and six patients had 3rd nerve involvement with absent gag reflex (Group C). Out of 63 patients, 90% required ventilation due to respiratory paralysis. Mean duration of hospital stay in Group A was 130.42 h, mean duration of intubation was 86.43 h and mean duration of ventilation was 81.63 h. In Group B patients hospital stay was prolonged (181.32 h), with prolonged intubation 139.93 h and longer period of ventilation 104.96 h. In Group C patients the hospital stay was 136.82 h, duration of intubation was 96.3 h and duration of ventilation was 93.27 h, which was more than Group A.
Conclusion: Patients requiring prolonged intubation, ventilation and longer hospital stay usually have more than one cranial nerve involvement. This can be used as an important clinical indicator of severity.

126. Scorpion envenomation management at King Khalid General Hospital Al Majmaah, Saudi Arabia: A study of 254 cases

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Objective: Scorpion envenomation is an accident which is raging across the five continents. Its frequency and its morbi-mortality are a public health problem in many countries of North Africa, India and the Middle East. The objective of our study is to investigate the epidemiology and the management of scorpion envenomation at King Khalid general Hospital Al Majmaah, Saudi Arabia.

Methods: A retrospective study of all cases of scorpion sting presenting at our hospital from 1 January 2011 to 31 December 2012.
Results: 254 cases were reported. The vast majority of incidents occurred in the warm season (82.7%) and in rural areas (83.1%). The majority of patients were males (87%). Mean age was 32.6 ± 12.6 years. The color of the scorpion was black in 68.1% and yellow in 24.4%. Most of the stings were on the upper limbs in 22% and lower limbs in 53.5%. The mean time between the scorpion sting and arrival at the emergency room was 1.5 h. The commonest symptom was pain (82.7%). The most common local signs were sting marks (33.9%), edema (18.9%), and redness (53.5%). The systemic signs were tachycardia (7.1%), hypotension (9.4%), abdominal pain, nausea and vomiting (31.9%), hyperthermia (16.5%) and pulmonary edema in three cases. The most frequent biological disorders were leukocytosis (17.7%), anemia (2.8%), hyperglycemia (7.5%), and hyperkalemia (3.1%). At the scene of the accident, 100 patients (39.4%) received first aid: local incision (11%), use of a tourniquet (12.2%), suction (15.4%). Analgesics were given to 190 patients (74.8%) and steroids were used in 9 cases (3.5%). All 254 patients received anti-tetanus serotherapy and polyvalent anti-venom. No anti-venom adverse effect was seen. 53.5% of patients were admitted. The mean duration of hospitalization was 1.5 days. Seventy-one patients (28%) were observed in the emergency room. Systemic complications were seen in 23 cases (9.1%). No fatal case was recorded in our series.
Conclusion: Having the anti-venom available in family health care centers and educating rural men about the hazards and treatment of scorpion stings and the importance of rapid transfer to a medical center, may help to decrease morbidity resulting from scorpion stings in the region.

127. Clinical consequences of scorpion stings in Campinas, São Paulo State, Southeastern Brazil

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Objective: To describe the clinical consequences of scorpion stings in the region of Campinas, southeastern Brazil.
Methods: A retrospective study of individuals stung by scorpions and treated at the university teaching hospital from 1994 to 2011 was undertaken. The clinical classification based on an international consensus[1] was: dry sting (no envenoming), class I (only local manifestations), class II (systemic manifestations), class III (life-threatening systemic manifestations such as cardiac and/or respiratory failure), and lethal.
Results: During this period, 1327 cases of scorpion sting were treated at the university hospital. The median age of the patients was 27 years [interquartile interval (IQI) = 15–42 year], and the scorpion species was identified in 47.2% of cases (*Tityus bahiensis*: 27.7%; *Tityus serrulatus*: 19.5%). The clinical classification was: dry stings (3.4%), class I (79.6%), class II (15.1%), class III (1.8%) and lethal (0.1%). Pain (95.5%) was the main local manifestation. Systemic manifestations such as vomiting (generally frequent and profuse), tachypnea, dyspnea, diaphoresis, tachycardia/bradycardia, prostration/agitation, pallor, and hypothermia were associated with greater severity of envenomation. Class III (n = 24) and lethal (n = 1) cases were restricted to children < 15 years of age (median = 4 year, IQI = 2–8 year) and, when the scorpion was identified (n = 13/25), primarily with *T. serrulatus* (n = 12/13). In 44 children with intense systemic manifestations (class II = 20, class III = 24), there was a similar profile of laboratory alterations upon admission, namely, hyperglycemia, hypocalemia, leukocytosis, elevated blood lactate, and compensated metabolic acidosis. However, elevations in serum total creatine kinase (CK), CK-MB and troponin, and echocardiographic alterations such as a decrease in the ventricular ejected fraction were significantly more common in class III cases. Seventeen patients developed pulmonary edema and 16 had signs of cardiac failure. The main therapeutic approaches used were: local anesthesia/analgesics (82.4%), scorpion antivenom (6.8%), dobutamine (1.7%), furosemide (1.0%) and mechanical ventilation (1.3%).
Conclusion: Most scorpion stings in the region of Campinas caused only local manifestations, mainly pain; the greatest severity was associated with stings by *T. serrulatus* and in children < 15 years.

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128. The knowledge of receiving antivenom is more effective than antivenom or analgesia for treating latrodectism

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Objective: We aimed to quantify the effect of patients knowing they would receive antivenom for treating widow spider envenoming (latrodectism).
Methods: Data were taken from two blinded randomized controlled trials of antivenom for latrodectism. The first was a controlled trial of intramuscular versus intravenous antivenom (RAVE-I)[1] where all patients knew they would get antivenom and only received rescue analgesia after antivenom. The second study (RAVE-II) was a placebo controlled trial of antivenom where half of patients receive intravenous antivenom but all patients receive standardized analgesia (paracetamol[1 g], ibuprofen[800 mg] and oxycodone[5–10 mg]) at enrolment. In RAVE-II patients knew they may not receive antivenom. We compared outcomes between trials to determine whether knowing if antivenom was given might influence outcomes. The primary outcome for both trials was clinically improved pain 2 h post-antivenom.
Results: There were 126 patients in RAVE-I and 224 in RAVE-II; both studies were negative. There were no differences in baseline characteristics between trials (Table 1). Pain was clinically improved in 67/126 (53%) in RAVE-I compared to 64/224

Table 1. Baseline characteristics in RAVE-I and RAVE-II.

	RAVE-I	RAVE-II
Number	126	224
Female	77 (61%)	114 (51%)
Age (years)	39 (IQR: 32–50)	39 (IQR: 29–54)
Baseline pain score	6.3 (4–7.7)	7 (5–8)
Systemic features	55 (44%)	76 (34%)
Difference at 2 h	3.7 (1.6–6)	2 (0.75–3.25)
Improved pain	73 (58%)	64 (29%)
Improved systemic effects	34 (62%)	18 (24%)

(29%) in RAVE-II (relative risk [RR], 1.9; 95% CI:1.4–2.4; $p < 0.0001$). In patients with systemic envenoming, there was a resolution of systemic effects at 2 h in 34/55 (62%) in RAVE-I compared to 18/76 (24%) in RAVE-II (RR 2.6; 95% CI: 1.7–4.1; $p < 0.0001$).

Conclusion: The knowledge of receiving antivenom significantly affected outcomes in latrodectism. The belief antivenom was given was twice as effective as analgesia for pain, and 2.5-times more effective for treating systemic effects.

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129. Toxicosurveillance of Novel Psychoactive Substances: An emergency department perspective and the role of the European Drug Emergencies Network (Euro-DEN) project

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Introduction: The last decade has seen significant changes in the pattern of substances available and used on the recreational drug scene. Alongside the continuing use of classical recreational drugs such as cocaine, amphetamine type stimulants and ketamine, there has been a large increase in the availability of novel psychoactive substances (NPS, known incorrectly by users and some professionals as "legal highs"). Through the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) Early Warning System, there is now detection of at least one new substance per week in Europe in both 2012 and 2013.[1]

Discussion: It is important not only for healthcare professionals treating those with acute toxicity (harm) associated with the use of recreational drugs and NPS, but also legislative authorities making decisions regarding the legal status of NPS, to have accurate information on the expected pattern of acute toxicity of new individual substances and/or classes of NPS. In Europe, there is currently no robust systematic system for capturing this information on the pattern of acute toxicity associated with the use of NPS. There are a number of different data sources currently available, including user self-reports on Internet discussion fora, user surveys (both Internet based and face-to-face interviews), case reports and/or case series and data from poisons centers or poisons information services.[2,3] There are a number of studies which clearly demonstrate that the content of recreational drugs and NPS is variable.[4,5] Therefore the information from these sources is often limited by the fact that the reported substance(s) may not have been the one(s) that were actually used. Individuals with acute toxicity related to the use of recreational drugs and/or NPS often present to a hospital emergency department (ED) or similar facility for management. The above sources of information on acute toxicity typically do not collect systematic data on presentations to an individual or network of ED(s). The coding systems used currently are based on the International Classification of Diseases version 10 (ICD-10), which does not have diagnostic codes for a number of recreational drugs or any of the NPS. In addition over 50% of individuals with acute toxicity are discharged directly from the ED, and will not be captured as clinical coding only occurs in many countries for episodes where the patient is admitted to hospital. Therefore it is not possible to use information collected at a regional or national level to monitor trends in presentations to EDs with acute toxicity from recreational drugs or NPS. While some data may be available from individual EDs across Europe and there are examples of local networks in specific regions within an individual country, to date there has been no system for collecting data from multiple EDs across different European countries. The European Drugs Emergencies Network (Euro-DEN) project was established not only to address these deficiencies in data on the acute harms related to recreational drugs and NPS. It was funded through the 2012 European Commission Directorate-General Justice Drug Prevention and Information Programme. The overarching objective of the Euro-DEN project is to develop a network of sentinel centers across Europe with specialist clinical, toxicological and research interests in the adverse consequences of recreational drugs and NPS. Through this network, data will be collected over a 12-month period to determine the epidemiology of presentations to the Emergency Department with acute harm from recreational drugs and NPS from across Europe, which will reduce knowledge gaps in this area.

Conclusion: The Euro-DEN project will use the data collected from the network to inform the content of a training package to improve the identification and management of acute recreational drug and NPS toxicity by staff working in recreational settings.

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130. Integrating mechanistic research for management of toxic alcohol poisoning

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Background: Diethylene glycol (DEG) has produced numerous mass poisonings worldwide, primarily because it has been mistakenly used as a solvent in drug formulations. DEG poisoning can result in acute renal failure, moderate liver toxicity and peripheral neuropathy. 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. Recent studies have convincingly shown that a metabolite of DEG is responsible for producing the renal toxicity and that a heretofore undetected metabolite, diglycolic acid (DGA), is the likely toxic metabolite. In cultured human proximal tubule (HPT) cells, DGA induces a marked degree of necrotic cell death, which is preceded by a depletion of adenosine triphosphate (ATP). Further studies have examined the toxic mechanism of DGA and offer possible therapeutic interventions for DEG poisoning.
Methods and results: HPT cells pretreated with DGA for 6 h showed a concentration-dependent decrease in oxygen consumption suggesting interference with the mitochondrial utilization of oxygen. DGA (50 mmol/L) treatment of HPT cells dissipated the mitochondrial membrane potential (MMP) with significant inhibition by 12 h. Co-incubation of cells with DGA and the antioxidant, α-tocopherol, significantly reduced DGA-induced reactive oxygen species (ROS) formation, but did not reverse the effects on the MMP nor on the measures of necrotic cell death. DGA treatment also significantly and preferentially inhibited succinate dehydrogenase activity, but had no effect on other citric acid cycle enzyme activities. *In vivo*, DGA is known to be concentrated 100-fold into kidney tissue, presumably by dicarboxylate transporters localized to proximal tubule cell membranes. 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.
Conclusion: These data indicate that DGA produces proximal tubule cell necrosis via a molecular mimicry mechanism that promotes enhanced renal accumulation and mitochondrial dysfunction (DGA is a four-carbon, dicarboxylic acid with structural similarity to Krebs cycle intermediates). Although inhibition of DEG metabolism would be therapeutic if applied early in this poisonings, availability of fomepizole or ethanol can be limited in mass poisonings. Alternatively, development of small molecules that alter the cellular accumulation of DGA uptake or that counteract its effects on mitochondrial metabolism might be useful in the therapy of DEG poisoning.

131. Carbon monoxide release curves from measurements during indoor charcoal burning: Systematic research on toxic levels for humans

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Objective: The Federal Institute for Risk Assessment (BfR) DocCenter has received more and more reports of cases of carbon monoxide (CO) poisoning, some even with fatal outcomes after indoor use of charcoal grills. CO is odorless, colorless, non-irritant and does not produce any other warning effect perceptible to humans. The BfR and the Federal Institute for Materials Research and Testing (BAM) have completed a cooperative research project to investigate the toxic concentrations of CO that are reached when charcoal grills or open fires are used indoors.
Methods: The first test series were conducted in a 1 m^3 measuring chamber. Since the situation of larger interiors could not be reproduced, additional measurements had to be taken (with 800 g of glowing charcoal each) in a larger cloud chamber with a spatial volume of 19 m^3. This chamber provides a good model for a small garage or a living room. CO concentrations were measured both under the ceiling and in the immediate vicinity of the grill. Systematic experiments were conducted. The data collected provided the basis for additional computer simulations, where the distribution of CO in rooms of any size could be calculated
Results: The glowing charcoal releases considerable amounts of toxic gases, notably CO. Based on calculations in a closed garage where 800 g of charcoal are burned for 30 min, CO concentrations of between 750 and 1100 ppm (parts per million) are to be expected. Based on clinical data, 200 ppm of CO in the ambient air causes slight headaches after 2 h. At 800 ppm, dizziness and nausea are experienced. After about 2 h of exposure to such a concentration, humans lose consciousness. Within no more than 2 h of glowing embers from 800 g of charcoal, CO concentrations exceeding 3000 ppm were measured, which are fatal for humans after a few minutes.
Conclusion: According to the release curves, dangerous carbon monoxide levels are already reached within a relatively short time. Even when windows, doors and the garage door are opened for "safety reasons", fatal CO concentrations can build up rapidly. It is strongly recommend that no burning materials such as charcoal are used indoors as a heat source for grilling, cooking or heating.

132. How often do North American crotalid bites need surgical management?

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Objective: Snake envenomations are a frequent cause of presentation to the emergency department (ED) in parts of the United States. Due to concern for compartment syndrome, these patients are often admitted to a surgical service. Given the safety of newer antivenoms and the rarity of compartment syndrome complicating envenomations by North American Crotalinae, we reviewed the outcomes of all patients presenting to the ED over the last 4 years.
Methods: This study is a retrospective analysis of surgical outcomes and complications of North American snake envenomations of pediatric and adult patients in an academic referral center

during a 4-year period. All snakebites receiving toxicology consults were recorded in a local database at a Level 1 trauma center and co-located tertiary care children's hospital. All consults were initially evaluated in the ED. Patients were excluded if there was not clear physical evidence of snakebite. We recorded the proportion of cases managed without admission to a surgical service and the frequency of cases receiving surgical intervention.
Results: From 2010 to 2013, 45 snakebites were evaluated and no cases required emergency surgery (fasciotomy, aggressive debridement). One case involved a minor dermotomy of the finger, 36 (80%) received antivenin, with 16 (35.6%) receiving repeat dosing of antivenin. Sixteen of nineteen adult patients were monitored in the observation section of the ED and discharged without requiring formal admission. No patients developed systemic coagulopathy, although one adult was admitted to the intensive care unit with intubation from airway compromise secondary to systemic effects of the bite. The mean length of stay for all 45 patients was less than 2 days.
Conclusion: Although compartment syndrome is often a concern for snakebites to extremities, surgical intervention is rare. Most patients can be appropriately managed in an ED observation or general medical/pediatric service with management guided by a medical toxicologist.

133. Weever fish envenomation: Analysis of enquiries to the Poisons Information Centre Erfurt from 1994 to 2013

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Background: Weever fish (9 species in 2 genera) have poisonous spines on their first dorsal fins and gills and are mostly restricted to the eastern Atlantic and the Mediterranean Sea. Although only one (Mecklenburg-West Pomerania) of four federal states the Poisons Information Centre (PIC) Erfurt is serving borders on the Baltic Sea, the PIC Erfurt receives several enquiries every year about weever fish envenomations.
Methods: In a retrospective study the yearly frequencies, symptoms, age groups, and regions of weever fish envenomation related enquiries to the PIC Erfurt from the beginning of 1994 to the end of October 2013 were analysed.
Results: In total, 44 weever fish envenomations were registered (yearly mean 2.2, range 0–7). Adults (90.9%) were more often stung by weever fish than children (9.1%) and males (68.2%) more frequently than females (22.7%). Typically, weever fish envenomations occurred in holidays during leisure time activities like wading through shallow water, swimming or fishing. Main regions of weever fish envenomation were the Mediterranean Sea (10/44), the Atlantic Ocean (7/44), and the North Sea (3/44). Only two cases of weever fish envenomation were reported from the Baltic Sea. The PIC Erfurt was contacted mostly a few days after envenomation (median: 6 days) and continuing symptoms were always reported. Most frequent symptoms were local pain (18/44), swelling and oedema (22/44) in hands (18/44) or feet (9/44), sometimes affecting the whole limb, and undefined local reaction (8/44). Cardiovascular symptoms were collapse (2/44), tachycardia (1/44), and hypotension (1/44). In one case, wound healing was complicated by a persisting sting and in another by an erysipeloid reaction. In five cases, treatment of weever fish envenomation included hot water immersion (not recommended by the PIC Erfurt) and was mostly supportive like wound disinfection, assessment of tetanus vaccination, administration of analgesics, antihistamines, glucocorticoids, and antibiotics.
Conclusion: Mainly due to tourism, the PIC Erfurt received several enquiries per year about weever fish envenomation. Mostly, hands and feet were affected during swimming and fishing and symptoms lasted for a few days. No evidence based treatment of weever fish envenomation exists. Complications of wound healing are persisting stings or secondary infection.

134. Magnetic resonance appearance of the brain in snake bite patients: Resonating the venomous findings

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Objective: Snake bite is a common cause of morbidity in the Indian subcontinent. Snake venoms with neurotoxic activity produce paralysis and respiratory distress, resulting in hypoxic damage. This study was carried out to evaluate Magnetic Resonance Imaging (MRI) brain injuries in victims of snake envenomation.
Methods: Patients with a history of snake bite during the previous 48 h presenting to the emergency service over 6 months were included. MRI was performed in patients presenting neurological symptoms. MRI protocol included T2-weighted axial, 3D-T1-weighted MPRAGE/SPGR, T2-FLAIR-weighted axial, diffusion-weighted axial, 3D-susceptibility-weighted sequences, 3DTOF-MR angiography (MRA) and 2DTOF-MR venography (MRV). Results were interpreted by two experienced radiologists and compared with clinical outcome
Results: Of the 35 included patients, 25 developed neurological complaints. Only ten patients could be taken up for MRI, six were bitten by a neurotoxic snake *Bungarus caeruleus*, one by a vasculotoxic snake (*D. russelii*) while in the remaining three, the snake could not be identified despite a picture akin to common krait envenomation. Victims presented with acute flaccid paralysis and respiratory involvement. Vasculotoxic snake envenomation resulted in local swelling and necrosis followed by disseminated intravascular coagulation and renal dysfunction. Four patients showed hypoxic ischemic changes, including global hypoxia secondary possibly to respiratory/cardiac arrest (N = 2) and scattered ischemic changes as diffusion restricting T2-hyperintense lesions in the white and deep grey matter (N = 2). These changes were seen in patients with *B. caeruleus* envenomation. MRI was normal in five patients. MRA showed diffusely attenuated intracranial arterial circulation in two patients with neuroparalytic snake envenomation, who had developed cardiac arrest. MRA was normal in eight patients. MRV was normal in all patients.

Conclusion. In this case series highlighting MRI neurological manifestations of snake bite, the various causes of hypoxic-ischemic sequelae could be global hypoperfusion/hypoxia secondary to neuroparalysis in neuroparalytic snake bites, thrombotic vascular occlusion in vasculotoxic snake bites, and transient flow cessation following cardiac arrest in either of the varieties.

135. Incidence and severity of hypotension and bradycardia in ciguatera

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Objective: To determine the incidence and severity of hypotension (systolic blood pressure < 100 mmHg) and bradycardia (heart rate < 60 beats per minute) in ciguatera based on the experience of three general hospitals in Hong Kong during 2003–2006.
Methods: Adult cases of ciguatera requiring treatment in the Prince of Wales Hospital (PWH) and two published case series from two other hospitals[1,2] were reviewed.
Results: Patients generally developed gastrointestinal and/or neurological signs and symptoms. In addition, five of the six PWH patients developed hypotension and sinus bradycardia. In two patients,[3,4] hypotension was prolonged, requiring intensive care unit (ICU) care for 2–3.5 days and intravenous infusions of dopamine, fluids and plasma volume expander. In the two published case series, all 12 adults developed hypotension and bradycardia (sinus bradycardia in 10, junctional bradycardia in 1 and Wenckebach second-degree AV block in 1), but none required ICU care. The reef fish species responsible for these local outbreaks included coral grouper, lyretail, and black fin red snapper.
Conclusion: In ciguatera, hypotension and bradycardia were much more common than generally realized, and the hypotension could be prolonged.

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136. Complement cascade activation by *Bothrops lanceolatus* venom: A "pathway" to improving patient management in case of envenomation?

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Objective: *Bothrops lanceolatus*, commonly named "Fer-de-Lance", is the endemic snake of the French Caribbean Island Martinique, where it is responsible for about 20–30 bites per year. *B. lanceolatus* venom (BlV) causes systemic thrombotic syndrome, resolved by specific antivenom injection, but also important local inflammation, involving extensive oedema, pain, and hemorrhage from fang punctures. It was recently described that several bothropic venoms from South America activate the complement system and that metallo and/or serine proteinases are involved in this process.[1] In the present study we investigated the complement cascade activation potential of BlV, in order to understand the mechanism of local lesions and maybe establish the basis for improving the treatment of local symptoms in case of envenomation.
Methods: We used electrophoretic separation, fluorimetric enzymatic assays, in addition to immunochemical assays to study BlV.
Results: Components of BlV share antigenic similarities with South American Bothrops species, since the therapeutic antibothropic antivenom raised against Brazilian snakes cross-reacted with the venom in Western blot and ELISA assays. Furthermore, Western blot analysis using lectins highlighted the presence of glycosylated proteins, which may activate complement cascade via the lectin pathway. This activation was confirmed by ELISA testing the binding of C4. Hemolytic assays showed that BlV activates the complement cascade also by both alternative and classical pathways. Furthermore BlV is able to directly cleave purified human proteins C3, C4, C5, and C1Inh, releasing anaphylatoxins C3a, C4a, and C5a.
Conclusion: These data indicate that BlV activates the complement cascade via classical, alternative and lectin pathways, a fact that could play an important role in the local inflammatory reaction and hemostasis disturbance caused by BlV, via a strong release of anaphylatoxins. More investigations are still needed to identify the proteases involved and their mechanisms of action on complement, however the present data suggest that the mechanism could be similar to what was described with other bothropic venoms.

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137. *Vipera berus* bite causing compartment syndrome in a 14-year-old boy

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Objective: *Vipera berus* (Vb) is a common snake in Austria. Its bites can cause severe symptoms in children, therefore administration of antivenom should be considered early. It is mostly effective when given within 18 h.[1] We report a case of Vb bite in a boy who received no antivenom.
Case report: A 14-year-old previous healthy boy was bitten on the proximal phalanx of the right index finger by a Vb while playing in an alpine pasture in Styria. Shortly thereafter, his father drove him to the nearest regional hospital. On arrival at the intensive care unit symptoms were: local pain, blue local skin discoloration and edema of the hand. One and a half hours later the patient complained of abdominal cramps and vomited twice. Ten hours after the bite the edema spread proximally and reached the upper arm. The laboratory showed C-reactive protein elevation (16 mg/L),

leucocytosis (14.26 G/L), a slightly decreased prothrombin time (68%), increased international normalized ratio (1.31). Therapy during the first 2 days: antibiotics, thrombosis prophylaxis, local cooling, analgesics, benzodiazepines, immobilization of the arm. Due to the progression of pain in the arm, edema up to the thorax, development of hyposensibility in the area of Nervus ulnaris and medianus the boy was transferred to a University Hospital where acute compartment syndrome was diagnosed. On day 2 the Poisons Information Center (PIC) was consulted once. The boy´s hand and forearm required emergency fasciotomy with multiple surgical revisions and a vacuum-assisted wound closure therapy afterwards. At the time of discharge the boy still complained of pain, sensory disturbances, restricted mobility in his right forearm and hand.
Conclusion: In case of snake bite it is recommended to consult the PIC as early as possible in order to decide whether the administration of antivenom is indicated according to the established expert opinion.[2]

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138. Scorpion stings in Mali: Epidemiological aspects

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Objective: Scorpion envenoming is a major public health problem in many tropical and subtropical countries. The aim of this study is to determine the frequency and the epidemiological features of scorpion stings in Mali.
Methods: This is a descriptive retrospective analysis of scorpion sting cases, recorded between 2001 and 2009 in the Gao and Kidal hospitals.
Results: A total of 413 scorpion sting cases were recorded during the study period. Of these, 54.5% were in health reference centers, 38.7% in military hospitals and 6.8% in regional hospitals. The cases occurred principally in the warmer months and between 10 h and 18 h in 65.6% of cases. More than three-quarters were males with a male-female ratio of 4. The average age of the patients was 31 ± 12 years. According to the results obtained, 7.4% of victims were under the age of 15 years. In 58.5% of cases, the sting was on the upper limb, 40.5% on the lower extremity and 1% on the trunk. The median delay in presentation to hospital was 4 h. Among the 148 patients for whom the outcome is known, 4 of them died.
Conclusion: Scorpion envenomation is a serious public health threat in Mali due to the presence of dangerous species: *Leiurus quinquestriatus, Androctonus australis,* and *Androctonus amoreuxi*.

139. Envenomation by a sea anemone on the French Atlantic Coast

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Objective: Envenomation by cnidarians have been a recurring problem on the Atlantic French coast since 2008.[1] Data from the Bordeaux Poison Control Center show most cases involve jellyfish. However, other cnidarians are present and can result in relatively severe poisoning, especially in children. We report the case of a 2-year-old child who was stung by a sea anemone.
Case report: A 2-year-old girl was playing on the beach at low tide on the Bay of Arcachon without a swimsuit and accidentally sat on a sea anemone. She immediately developed a very intense pain with crying and restlessness. She was drowsy for approximately an hour after the sting. On examination she had very large skin lesions on the buttocks but the perineum remained unaffected. She was discharged with antihistamine and analgesic treatment. She represented 48 h later, however, and the lesions had become red, and oozing, accompanied by a fever of 38.5°C. Maculopapular lesions were apparent over the entire posterior surface of the thorax. The child was given prednisolone 1 mg/kg for 15 days. Although the lesions gradually disappeared, dark red marks were still clearly visible 3 months later. Several species of sea anemone are found on the Atlantic seaboard (*Anemonia sulcata*, *Corynactis viridis*, *Urticina felina*, *Actinothoe sphyrodeta*) and they all have a typical venomous harpoon-like device for delivery of venom. The venom contains a protein that affects potassium channels. According to the size of the animal and the description given by the parents, *Anemonia sulcata* is suspected in this case.
Conclusion: Envenomation with severe dermatological lesions has not previously been reported from sea anemones on the French Atlantic coast, although a series of cases has been described on the Adriatic Sea.[2] The child presented mild systemic symptoms immediately, and fever the following day.

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140. *Bitis arietans* envenomation in snake charmers in the Province of Tiznit, Morocco: First two case reports

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Objective: Snake charmers in Morocco often handle *Bitis arietans*. A bite from this species can result in severe envenomation. To date, there have been no published case reports of envenomation by this viper in Morocco. We report two cases of *Bitis arietans* envenomation in snake charmers in the province of Tiznit in the South of Morocco. To our knowledge, these are the first reported cases.
Case series: Case 1: The patient was a 46-year-old male snake charmer with no significant prior medical history, who sustained a bite in the left hand while handling *Bitis arietans*. He was admitted to the intensive care unit 4 h after the bite and presented with significant local pain and bleeding at the bite site, edema extending to the arm with progressive ecchymosis. The symptoms improved after administration of three vials of Fav-Afrique®. Case 2: The patient was a 31-year-old snake charmer with a history of eight prior *Bitis arietans* bites between 1991 and 2012. The bite was at the anterior area of the left leg and the patient had leg edema that extended to the thigh. The coagulation time was normal. Patient refused treatment with Fav-Afrique®. Symptoms improved with symptomatic care.
Conclusion: *Bitis arietans* venom causes inflammation, necrosis and hemorrhage. The snake charmers handling these snakes need to be educated about the potential complications of an envenomation.

141. Risk profile *Vipera berus* bites

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Objective: *Vipera berus* is the only poisonous snake in Germany. Snake bites are perceived as threatening events and they frighten the patients. Hence, poisons centers are consulted regularly regarding these cases. The aim of this analysis is to give an overview of viper bites in eight federal states of Germany and the identification of high-risk groups for the exposure to viper bites and for the occurrence of severe symptoms.
Methods: Retrospective analysis of all cases of viper bites of two German poisons centers over a period of 17 years concerning demographic data and symptom severity according to the Poisoning Severity Score (PSS).
Results: From 1996 to 2012 the poisons centers collected 448 cases of snake bites which met the inclusion criteria. The average age was 30.6 years. Males were bitten more than twice as often as females (m/f = 2.1/1). The highest risk of getting bitten affects the group aged 20–49 years. In this group also occurs the highest difference in the gender ratio (m/f = 2.6/1). More than 60% of the cases were observed during June, July, and August. Nearly one fourth of all bites (24.6%) were reported in July. Concerning the time of day 25% of the bites occurred between 2 and 4 pm. With more than 30 recorded bites in Saxony near Dresden and the coastal regions of Mecklenburg-West Pomerania showed the highest rates of viper bites. Symptom severity was: 24 asymptomatic (5.4%), 318 minor (71.0%), 90 moderate (20.1%) 4 severe (0.9%), and 13 not documented (2.8%). Infants from 1–4 years of age (31.5% in this group) and seniors over 70 years (50.0% in this group) were at the highest risk for developing moderate and severe symptoms.
Conclusion: *Vipera berus* bites are a steady source of envenomation in Germany. Males are bitten more often than females. Infants and seniors are at a higher risk of developing moderate and severe symptoms. Therapy is a specific antivenom which is only used in severe cases, otherwise therapy is symptomatic.

142. Compartment syndrome after a bite by the South American rattlesnake (*Crotalus durissus terrificus*): Case report

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Objective: To report the outcome of a patient who developed compartment syndrome after a bite by *Crotalus durissus terrificus*.
Case report: A 63-year-old male was admitted 1 h after being bitten on the right elbow by a "large" snake (not brought for identification). Physical examination revealed two fang marks 1.5 cm apart, local tense swelling, erythema, paresthesia and intense local pain (10/10, visual analog pain scale). The main laboratory findings upon admission were incoagulable blood (incoagulable prothrombin time (PT), activated partial thromboplastin time (aPTT) and international normalized ration (INR)) and serum creatine kinase (CK) of 1530 U/L (RV < 170 U/L). Based on the clinical and laboratory features the case was classified as moderate/severe envenoming probably caused by an adult *Bothrops* spp. snake, with imminent compartment syndrome as a possible complication. The patient was treated with 80 mL of bothropic antivenom (AV), limb elevation and morphine, but initial evolution revealed no improvement in the local pain and coagulopathy. The patient also developed neuromyotoxic manifestations, including muscle weakness, palpebral ptosis and rhabdomyolysis (CK = 126 160 U/L, 14 h post-bite), suggestive of severe envenoming caused by *C. d. terrificus*, and was treated with 200 mL of crotalic AV (15 h post-bite) and fluid replacement. Magnetic resonance imaging (MRI) at 24 h post-bite detected marked edema of the anterior compartment of the right forearm; a high anterior compartment pressure (40 mmHg) was observed 25 h post-bite, as measured with a needle/catheter connected to a calibrated (zeroed) pressure monitor device (Stryker™). ELISA revealed a high serum concentration of *C. d. terrificus* venom (54.1 ng/mL, cut-off = 2.5 ng/mL) in a blood sample collected before AV infusion (1 h post-bite); the assay was negative for *Bothrops* venom (cut-off = 2.3 ng/mL). No fasciotomy was performed and the patient was discharged 6 days after receiving rattlesnake AV, without sequelae.

Conclusion: Compartment syndrome is an unusual but severe complication of bites by crotaline snakes such as North American rattlesnakes and *Bothrops* spp. snakes. To our knowledge, no previous study has reported compartment syndrome after bites by *C. d. terrificus*. In agreement with other reports from our group, MRI in conjunction with subfascial pressure measurement may be useful in diagnosing compartment syndrome after snakebite.

143. Serum sickness after the administration of Australian snake antivenoms

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Objective: To investigate the frequency of serum sickness following the administration of Australian snake antivenoms.
Methods: This was a prospective cohort study of patients recruited to the Australian Snakebite Project (ASP) who received snake antivenom from November 2012 to September 2013. Demographics, clinical information, laboratory tests and antivenom treatment are recorded prospectively for all patients recruited to ASP and in addition these patients were telephoned 7–10 days and 6 weeks after administration of antivenom. The primary outcome was the proportion of patients with serum sickness defined as 3 or more of the following characteristic clinical features, 7–21 days after antivenom administration – fever, erythematous rash, urticaria, myalgia/arthralgia, headache, malaise and nausea/vomiting.
Results: During the 11-month period 53 patients recruited to ASP received snake antivenom. One could not be contacted and one died within 24 h of admission to hospital. Fifty-one patients were followed up, 12 females and 39 males with a median age of 44 years (range: 11–77 years). The commonest reason for antivenom administration was venom induced consumption coagulopathy. The commonest antivenoms used were brown snake, tiger snake, and polyvalent antivenom. Serum sickness occurred in 20 of the 51 patients (39%).
Conclusion: Symptoms consistent with serum sickness were common following the administration of Australian snake antivenom. Further studies need to better identify cases of serum sickness and investigate potential treatments.

144. Cats experiencing toxicity after use of a new "Spot-on" pesticide product containing indoxacarb

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Background: The organophosphate and carbamate insecticides that were traditionally used in anti-flea products for pets have been replaced by less toxic compounds, for instance by indoxacarb, a broad-spectrum oxadiazine insecticide. Indoxacarb is a pro-drug that requires bioactivation by the insect enzymes to exert its toxic effects. The bioactivated metabolite acts as a voltage-dependent sodium channel blocker in the insect's nervous system.[1] Because mammals are much less efficient in their ability to convert indoxacarb into the active and toxic metabolite, it is claimed to be safe for mammals. Indoxacarb is sold as a spot-on product and is indicated for the treatment and prevention of flea infestation for dogs and cats.
Case series: The Dutch Poisons Information Center (DPIC) was contacted twice in 2012, and 11 times from January until October 2013, regarding cats with symptoms of toxicity after correct use of a "spot-on" product with indoxacarb. Mild to severe symptoms developed with ataxia, mydriasis, muscle weakness, muscle spasms, hypersalivation, vomiting, tachypnea, tachycardia, and hypertension. In two cases it was known that the cat had ingested the product by licking itself or another cat. It was reported that the time of onset of symptoms was 6–7 h after application, and no other cause was deemed responsible for these symptoms. A few veterinarians reported that the day after onset, the symptoms had diminished but the cats were still lethargic.
Conclusion: Indoxacarb is supposed to be safe for mammals and no toxic effects are mentioned in the information available at the site of European Medicines Agency (EMA). The EMA states that less than 5% of cats experienced mild adverse effects, consisting of excitation, anorexia, vomiting and excessive salivation. Oral exposure after licking was not expected to lead to toxicity according to this product information. The reported cases show significant effects after correct topical use. Based on post-marketing surveillance data, the safety of indoxacarb use in cats should be re-evaluated.

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145. Investigation of respiratory effects of norbuprenorphine and their modulation in the rat to define its contribution to buprenorphine toxicity

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Objectives: Asphyxia deaths and poisonings with respiratory depression have been attributed to buprenorphine (BUP), a maintenance treatment in heroin addicts. Previous works suggested that BUP toxicity could be attributed to its metabolite, norbuprenorphine (NBUP), mainly because of inhibition of the P-glycoprotein (P-gp), the NBUP efflux transporter at the blood-brain barrier. Intravenous misuse of crushed BUP pills represents one of the identified circumstances of BUP toxicity; BUP/naloxone (NLX) combination was thus recently marketed to dissuade misuse in drug addicts. Our objective was to study NBUP-related respiratory effects and their modulation by NLX in the presence of P-gp inhibition in the rat.

Methods: Respiratory effects were studied using plethysmography in Sprague-Dawley rats (with jugular catheters for intravenous drug administration) following NBUP administration (effect-dose relationships: 0.3–9 mg/kg), in the presence of NLX (combination of 3 mg/kg NBUP + 7.5 mg/kg NLX, according to 2:5 ratio) ± P-gp inhibitor (PSC 833 or valspodar, 10 mg/kg intravenously). Control animals received either the solvent (4% Tween) or BUP alone. For each animal and at each time, the difference between the value of the parameter at this time and at T = 0 (baseline) was calculated. Comparisons were performed using Mann–Whitney U-tests (2 groups) or one-factor ANOVA (3 groups).
Results: NBUP was responsible for deleterious dose-dependent respiratory effects (significant increase in inspiratory time and reduction in minute volume), prevented by the co-injection of NLX. PSC833 pretreatment increases not only NBUP- (significant reduction in minute volume) but also BUP-related respiratory effects (significant increase in BUP-induced inspiratory time).
Conclusion: In contrast to BUP, NBUP is responsible for a dose-dependent respiratory toxicity that is preventable by NLX co-administration. BUP/NLX combination may improve BUP safety in case of IV misuse, based on NLX-mediated prevention of NBUP toxicity, which is enhanced in the presence of P-gp inhibition.

146. High mobility group box 1 protein changes in serum of subjects exposed to irritant factors released during uncontrolled fire

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Objective: Evaluation of concentration of high mobility group box 1 protein (HMGB1) in serum from 40 patients hospitalized in the toxicological unit due to inhalational exposure to smoke from a fire.
Methods: Forty patients, hospitalized in the toxicological unit after exposure to toxic factors released during an uncontrolled fire participated in the project as a studied group. They underwent: spirometry, chest X-ray, evaluation of arterial blood gases, basal biochemistry tests: full blood count, urea and creatinine level. The HMGB1 concentration was measured in their serum samples at first day (day of admission), the second day, and the day of discharge. The HMGB1 concentration was also measured in the serum of blood samples from 10 unexposed, healthy persons (the control group).
Results: The average age of patients exposed to toxic factors released during uncontrolled fire was 49.75 years. The most frequent symptoms in the studied group were complaints associated with lower airways pathology reported by 21 (52.5%) patients, pharynx or nose-related symptoms occurred in 14 patients (35%), whereas symptoms suggestive of conjunctivitis were found in 9 (22.5%) patients. Statistically significantly higher levels of carboxyhemoglobin, thiocyanates, C reactive protein were revealed in comparison with the control group. No statistically significant changes in HMGB1 levels were found within the study group of 40 patients between the first day and other analysed days of hospitalization. Significantly higher HMGB1 levels were found on the first day within the group of patients complaining of at least one symptom (3.77 nanograms/mL) in a comparison with the control group (1.66 nanograms/mL).
Conclusion: The outcomes presented may indicate the usefulness of HMGB1 as a marker of exposure to toxic factors released during uncontrolled fire.[1]

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147. The antioxidant effect of Glehnia littoralis on α-amanitin induced hepatotoxicity

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Objective: *Glehnia littoralis* has been used for ischemic stroke, phlegm, cough, systemic paralysis, as an antipyretic and for neuralgia. The pharmacological mechanisms of *Glehnia littoralis* were reported as calcium channel blockage, anticoagulation, anti-convulsive effect, antioxidant, and anti-inflammatory effects until now. Alpha-amanitin is a powerful natural hepatotoxin that belongs to the amatoxins isolated from deadly poisonous *Amanita phalloides* mushroom. The alpha-amanitin generates free radicals, which may contribute to its severe hepatotoxicity. The aim of this study was to investigate whether *Glehnia littoralis* has a protective antioxidant effects on amanitin-induced hepatotoxicity.
Methods: The perpetual cell line (HepG2) which is derived from well-differentiated hepatocellular carcinoma cells was exposed to α-amanitin (AMA) and/or *Glehnia littoralis* extract (GLE), then activities of cells via MTT assay, superoxide dismutase (SOD), and catalase (CAT) were measured.
Results: The results showed that α-amanitin induced a significant decrease in cell viability and CAT activities. These processes were concentration dependent and statistically significantly different when compared to 2.0 mM α-amanitin exposure. The activity of SOD and CAT increased while the levels of malondialdehyde (MDA) and reactive oxygen species (ROS) decreased after treatment with GLE, while there were progressive benefits with increasing GLE concentrations. Thus, we supposed that *Glehnia littoralis* has a cell-protective effect. Hepato-toxicities caused by alpha-amanitin (2uM) were decreased according to the concentration of *Glehnia littoralis*.
Conclusion: In an *in vitro* model, *Glehnia littoralis* was effective in limiting hepatic injury after alpha-amanitin poisoning. Its antioxidant effect is attenuated by antidotal therapy.

148. Acid burns, comprehension of the lesions mechanism: The sulfuric acid example

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Objective: To understand concentrated acid lesions to the skin, such as lesions due to 98% sulfuric acid, with a simple efficient skin model.

Methods: Human skin explants obtained from elective abdominoplasties were preserved alive, sampled, fixed, and stained for histological observations. Control group: Untreated controls were sampled at the beginning of the experiment, and after 24 and 48 hours, 6 and 11 days. Sulfuric acid application: 30 µL of 98% sulfuric acid was applied by topical route on filter paper for various periods from 25 seconds to 48 hours to study sulfuric acid penetration; or applied for 25 seconds and sampled at 48 hours, 6 and 11 days in order to study spontaneous healing.
Results: For different times of application alterations, during penetration of sulfuric acid, were searched for in the stratum corneum, basal epidermis, papillary and reticular dermis. It allows an observation of the lesion progression throughout the skin. Obvious epidermal lesions and papillary dermis cellular alterations were observed at 3 min. From 4 to 48 hours of contact, severe epidermal lesions and obvious alterations in papillary and reticular dermis were observed. After a 25-second exposure and observations at 48 hours and 6 and 11 days, obvious epidermal alterations developed, and no regrowth was seen.
Conclusion: Under these operating conditions, the kinetics of 98% sulfuric acid burns can be precisely analyzed. This model completely corresponds to the clinical lesions observed during accidental splashes. The direct effect of the corrosive agent is extremely rapid and lesions progress very quickly. This study confirms the need for an urgent and effective decontamination to prevent or minimize the severity of chemical burns due to concentrated sulfuric acid.

149. Pilot study comparing hemodynamic measures and survival in swine anesthetized with alpha-chloralose and isoflurane

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Background: Cardiovascular toxin studies are hampered by synergistic effects of anesthetics. Alpha-chloralose (AC) is a gabaergic drug with minimal cardiovascular effects.[1] We sought to compare hemodynamic effects of AC with those of isoflurane in a swine model of nifedipine toxicity.
Methods: This Institutional Animal Care and Use Committee (IACUC)-approved study used 12 intubated, ventilated, and instrumented swine. All animals received AC (55 mg/kg bolus and 22 mg/kg/hour infusion) for instrumentation. After stabilization and basal measures, animals received AC without nifedipine (group 1), alternating AC and isoflurane with nifedipine (group 2), or AC with nifedipine (group 3). Group 2 animals received AC for 30 minutes, followed by 2% isoflurane and AC for 30 minutes, and AC was discontinued. After 30 minutes of 2% isoflurane only, it was decreased to 1% for 30 minutes. At the end of this period, isoflurane was stopped and AC restarted. Thirty minutes after AC restart, nifedipine was infused until animals were intoxicated. Once toxic, animals were again alternated between AC and 2% isoflurane for 30-minute periods. Student's t-test was used to compare the overall survival and hemodynamics with each anesthetic before and after toxicity.
Results: Isoflurane decreased mean arterial pressure prior to induction of toxicity (see Table 1). Once they became intoxicated, group 2 had shorter survival time than group 3 (83 ± 16 min vs. 232 ± 67.5 min, $p = 0.02$).
Conclusion: The choice of anesthesia for cardiovascular studies may impact hemodynamics and survival rates. Alpha-chloralose does not appear to augment nifedipine toxicity. Further comparison of isoflurane with AC is warranted.

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150. Phenethylamine poisonings reported in a French Poison Control Center

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Objective: During this last decade, psychostimulant drugs of the phenethylamine family have gained increasing popularity among recreational drug users.[1] Unfortunately, no series has yet been published by any poison control center (PCC) about phenethylamine poisoning. The aim of this retrospective study was to describe exposures to phenethylamines reported to the Angers PCC, their circumstances, and consequences.
Case series: Between January 2007 and December 2012, 77 cases of poisoning were selected, principally from western France. The

Table 1. Pilot study comparing hemodynamic measures and survival in swine anesthetized with AC and isoflurane.

	CO	SVR	SV	HR	MAP	CVP
Group 1 AC only	8.534 ± 2.74	803 ± 215	118 ± 28.5	72.0 ± 8.22	85.6 ± 13.2	5.11 ± 2.47
Group 2 AC only	8.05 ± 0.636	736 ± 41.7	147 ± 25.3	55.5 ± 6.36	92 ± 7.07	8 ± 0
Group 2 AC plus 2 % Iso	8.20 ± 3.39	550 ± 192	78.0 ± 15.6	102 ± 22.6	60 ± 4.24*	5 ± 1.41
Group 2 2% Iso only	6.40 ± 2.69	784 ± 353	65.5 ± 10.6	93.5 ± 30.4	66 ± 0*	7 ± 1.41
Group 2 1% Iso only	7.05 ± 2.12	734 ± 180	109 ± 46.7	66 ± 2.82	76 ± 12.7	7 ± 1.41

Iso = Isoflurane; CO = cardiac output (L/minute); SVR = systemic vascular resistance (dyne*s/cm^5); SV = stroke volume (mL); HR = heart rate (bpm); MAP = mean arterial pressure (mmHg); CVP = central venous pressure (mmHg)
*$p < 0.05$

sex-ratio (M/F) was 3.80 and the mean age was 26 ± 9 years. Among the products, MDMA (33 cases), amfetamine (15 cases), and metamfetamine (11 cases) were the most common. Synthetic cathinones (11 cases) and the 2C series (4 cases) were also found. The oral route was the preferred for administration (61% of cases), followed by nasal or inhalation (19%) and intravenous (10%) routes. In close to half of the cases, phenethylamines were taken alone. In the other cases, cannabis (27%), ethanol (20%), and cocaine (9%) were the most common drugs. Tachycardia (38%) and hypertension (14%) were the most frequently described cardiovascular symptoms, while anxiety and hallucinations (56%) have clouded the psychiatric picture; mydriasis and headache (44%) were frequent neurological symptoms. Complications such as seizures (n = 7), cardiac arrest (n = 4), toxic myocarditis (n = 1), and hemorrhagic stroke (n = 1) have been observed. The distribution of cases according to their Poison Severity Score[2] was as follows: PSS1: 49; PSS2: 17; PSS3: 6; and PSS4: 4. Seventy-eight per cent of the patients received hospital care and nine had to be admitted in an intensive care unit. Analytical confirmation was performed for all severe cases. While 94% of patients recovered, 4 patients died and 1 patient with neurological sequelae were observed.

Conclusion: Although their toxicity is underestimated by consumers, exposure to phenethylamines may be severe. Physicians, toxicologists and analysts should be alert for new trends in consumption in order to better evaluate these patients.

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151. Acute intoxications by new psychoactive substances: Patterns of use and circumstances of exposure EU Project SPICE II Plus

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Objective: Since 2008, hundreds of new psychoactive substances (NPS), among them synthetic cannabinoids (SC), emerged as recreational drugs. The aim of the investigation was to identify which NPS lead to consultation of emergency units because of undesirable effects and to identify patterns of use and circumstances of consumption.

Methods: Retrospective inquiry in the poisons center's (PCC) database (1/2008-6/2013), regarding the cases of human exposure to NPS, which lead to emergency medical treatment (EMT).

Results: A total of 263 patients were included, 190 after consumption of SC (age, 12–46 years; median, 18; male, 83%). Severity of poisoning was moderate or severe in 66%. Exposure by inhalation dominated (94%: water-pipe, 7%; joint, 87%). Consumption in a group was reported in 27% and polydrug use in 16% (predominantly ethanol, 10%). Seventy-three patients had consumed other NPS, and 59 of them cathinones (age, 18–55 years; median, 28; male, 97%). Severity of poisoning was moderate or severe in 76%. Routes of exposure were oral (54%), nasal (22%), or other (7%). Polydrug use was reported in 48% (predominantly illegal drugs; 1 patient also took SC). Fourteen patients took other NPS (12 different substances like 2C-E (3), 2C-D (2) [age, 13–57 years; median, 27; 79% male]), and polydrug use was observed in 20%. Poisoning severity was moderate or severe in 73%.

Conclusion: Acute intoxicated users of SC were almost 10 years younger on average than consumers of other NPS. One-quarter of users consumed SC in a group, without other kinds of NPS. Polydrug use was most common among the users of cathinones (48%). While the young and less experienced users of SC seem to be at special risk of developing acute poisoning, the acute intoxicated consumers of cathinones seem to be the most common long-term users of illicit substances. The groups barely overlap; only one patient had consumed SC plus cathinones. Data from intoxicated patients are a very important source for identifying certain substances as well as user groups and circumstances of consumption requiring EMT. Because retrospective data may be incomplete, we started a prospective evaluation in July 2013, as part of the EU Project SPICE II Plus.

152. Increasing illegal use of melanotan: The Barbie Drug hype

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Background: The illegal sale of non-registered drugs is an increasing problem. For example, melanotan products (promoted as Barbie Drug), synthetic analogues of alfa-melanocyte-stimulating hormone, are purchased via the Internet and injected to accomplish sunless tanning, sexual stimulation, or weight loss. In the clinical studies reported, side effects of melanotans I and II include nausea, fatigue, facial flushing, peripheral vasodilatation, and with melanotan II yawning and spontaneous penile erections. Before 2012, the Dutch Poisons Information Center (DPIC) was never consulted for these drugs, in 2012 once, and in 2013 five times.

Case series: Six patients (5 women and 1 man) reported adverse health effects after subcutaneous injection of melanotan II, bought in a Dutch webshop. A therapeutic dose (0.01 mg/kg) was taken once by one patient and during 5 days by another patient. The other 4 patients injected an overdose (up to 10x the recommended dose) once or repeatedly. The patients experienced nausea, vomiting, diaphoresis, dizziness, and angina pectoris. The male patient had an undesirable long-lasting erection. One patient injected an overdose during 6 days and the effects lasted for 1 week. The DPIC informed the responsible product safety authorities and the Dutch webshop withdrew the product.

Discussion: These cases illustrate that misuse or overdose of melanotan can result in toxicity. Dosing errors are common, probably because the products are sold as powders for subcutaneous

injection and users have to prepare a solution and calculate the required amount by themselves. Another health concern is that users inject the substance by themselves, without the supervision of a health professional. Infections may result from unprofessional administration.
Conclusion: Melanotan products are illegal and pose a health risk. Although one specific product is now withdrawn from a Dutch webshop, this product or similar products may still be available via other websites. Surveillance by poisons information centers is important for the early detection of emerging public health problems due to the marketed products. Collaboration between poisons centers and law enforcement authorities is essential to enable measures to prevent further damage to public health.

153. New psychoactive substances and illicit drugs used among 16-year-old high school students in Romania

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Objective: To obtain comparable data on knowledge, attitudes, and practices of high school students (16 years old) in the use of new psychoactive substances (NPS) and illicit drugs, thus making it possible to outline some trends in consumption patterns at this age.
Methods: This study is based on the data collected within the European School Survey Project on Alcohol and Other Drugs (ESPAD)[1] framework in 2011. The Romanian sampling frame included high school students in both grades 9 and 10, from 149 schools and 268 classes. The sampling frame has national representatives of students at regular schools and covered all 42 districts of the 8 regions. We investigated all the drugs considered illicit according to Romanian laws.
Results: The use of any type of illicit drug or NPS at least once in their lifetime was 19.2%, with the gender distribution as follows: 22.1% among boys and 16.8% among girls. The most frequently experimented drugs were cannabis and inhalants with a prevalence of 7.2% followed by NPS 5.3%. Regarding the age of onset of use of drugs, the highest rate of adolescents starting drug use was at the age of 13 or earlier in the case of inhalants: 1.8% of the total number, followed by cannabis and NPS: 0.8%. The risk of regular use, regardless of the drug type, is perceived as being high by most of the respondents, the proportions varying between 66% and 72%. The perception of high risk in the case of experimental use for the illicit drugs varied between 40% and 47% but only 28% for NPS. Of those who used illicit drugs, 69.1% have indicated curiosity as main motivation, 21.6% indicated the wish to change their mood, and 17% declared that they wanted to forget about their problems. The same classification was recorded in NPS use.
Conclusion: The result of the national study (ESPAD) ranks Romania in the last 10 European countries with regard to the level of prevalence of illicit drug and NPS use at least once in their lifetime among 16-year-old pupils.

Reference

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154. Urinary test for mephedrone/methcathinone in suspected intoxicated patients: Comparative evaluation between a new screening (ELISA) assay and liquid chromatography–mass spectrometry method

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Objective: Despite being marketed as "bath salts" or "plant food" and labelled "not for human consumption", people use synthetic cathinones for their amphetamine/cocaine-like effects. Within the National Early Warning System (NEWS), we compared the screening analysis in urine samples (using a mephedrone/methcathinone kit) with the liquid chromatography–mass spectrometry (LC–MS).
Methods: The study was conducted on 202 clinical urine specimens, collected from patients admitted to the national emergency departments, from April 2011 to April 2013. ELISA urine assay (Randox® Laboratories Ltd) was compared with urine LC-MS determinations (including detection of 13 parent cathinones, limit of detection 10 ng/mL, based on the availability of certified references standards).
Results: Of 195, 202 samples gave values < 7 ng/mL by ELISA screening, and tested negative by LC-MS. Seven urine samples showed concentrations of > 16 ng/mL by immunoassay, and only four of them resulted positive by LC-MS (2 for butylone, 1 for MDPV, and 1 for 4-MEC, mephedrone and pentedrone).
Conclusion: These data highlight a good global correspondence (positive + negative results) between the two analytical methods, showing disagreement in only 3 cases concerning positive results. At present, it is not possible to assess whether this disagreement can be related to a problem of interference/cross-reactivity of the ELISA assay, or to the presence of substance/metabolites not yet included in LC-MS standards. It is important to underline that the ELISA assay gave positive results in the 2 butylone-positive cases, even if this molecule is not reported in the cross-reactivities of the method. In this view, the screening can be considered a useful tool to rapidly detect these new psychoactive substances. The absence of false negative on the ELISA screening suggests the promising usefulness of this method in the emergency setting, even considering the current limit of the availability of reference standards for LC-MS.
Acknowledgement: Study supported by the Department for Antidrug Policies—Presidency of the Italian Council of Ministers.

155. Data evaluation from synthetic cannabinoids screening in biological samples by ELISA assay and liquid chromatography–mass spectrometry analysis

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Objective: Due to their reported cannabis-like effects, synthetic cannabinoid receptor agonists (SCARs) have gained much attention among young people. With respect to the continuous appearance of these new substances on the market since 2008, the development of reliable methods for the detection of these drugs including their respective metabolites in biological fluids has become essential. Within the National Early Warning System (NEWS), we carried out a screening analysis in urine samples using an enzyme-linked immunosorbent assay kit (ELISA) (Randox® Laboratories Ltd) together with a contemporary detection on blood samples with a liquid chromatography–mass spectrometry (LC-MS) screening method.
Methods: The ELISA assay was used for the detection of SCARs and their metabolites in urine, while LC–MS method was performed in blood for the detection of 21 parent SCARs based on the availability of certified references standards. The study was conducted in a total of 171 clinical biological specimens, collected from patients admitted to the national emergency departments, from April 2011 to April 2013.
Results: Out of a total of 171 cases, 147 urine samples tested with ELISA exhibited JWH-series values 5 ng/mL and negative LC-MS blood analysis (limit of detection, 0.2 ng/mL). Twenty-four samples gave urine concentration values of >7 ng/mL: among these, 16 blood samples resulted positive for at least one synthetic cannabinoid, and 8 samples were negative at LC-MS.
Conclusion: SCARs screening performed on two different matrices with two different analytical methods revealed disagreement in 8/171 cases (4.5%). This can be due to (i) pharmacokinetic aspects (ii) different targets of the two methods (parent drugs/metabolites in urine vs. parent drugs in blood), (iii) possible cross-reactivity of ELISA method with no-SCARs substances. These preliminary results support the use of urine screenings in the emergency setting to detect SCAR intoxications.
Acknowledgement: Study was supported by the Department for Anti-drug Policies—Presidency of the Italian Council of Ministers (2013).

156. Awareness and use of the NBOMe novel psychoactive substances is lower than those of mephedrone in a high drug using population

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Objective: The NBOMe group of compounds has novel psychoactive substances (NPS) which are N-o-methyoxybenzyl analogues of the 2C- phenethylamines. They have been detected in police seizures and case reports of toxicity related to NBOMe compounds, in particular 25-I NBOMe, have emerged from around Europe. However, there is limited data on the awareness of NBOMe and the prevalence of its use. Men who have sex with men (MSM) clubbers are considered to be "early adopters" of NPS with a higher prevalence of use;[1] the aim of this study was to determine the awareness and prevalence of use of NBOMe in MSM clubbers.
Methods: An anonymous questionnaire survey was carried out in three gay-friendly night clubs in South East London over two weekends in July 2013. Basic demographic data (age, sex, and self-identified sexual orientation) were obtained, together with awareness and previous use of mephedrone and NBOMe.
Results: Three hundred and ninety-seven participants completed the questionnaire; 89% were male, 75% MSM, and mean ± SD age was 30.1 ± 8.4 years. A significantly greater proportion had heard of mephedrone compared with NBOMe (96.0% vs. 11.8%, $p < 0.001$). Lifetime and last-month use of mephedrone were significantly higher than those of NBOMe (life-time use, 76.6% vs. 4.8%, $p < 0.001$; last-month use, 62.2% vs. 1.8%, $p < 0.001$). MSM were not more likely to have heard of NBOMe than of non-MSM (MSM: 10.5% vs. non-MSM: 15.8%; OR = 0.621 95% CI 0.324–1.192, $p = 0.149$). Similarly, MSM were not more likely to have tried NBOMe (4.7% vs. 5.0%: OR = 0.953; 95% CI, 0.335–2.716, $p = 1.0$) nor used within the last month (1.7% vs. 2%: OR = 0.851; 95% CI, 0.162–4.454, $p = 1.0$).
Conclusion: This study reveals that this high drug-using group has limited awareness of NBOMe compared to the more established NPS mephedrone. While MSM are considered to be early adopters of NPS, this group did not have greater use of NBOMe in this study.

Reference

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157. Detection of novel psychoactive substances through analysis of recreational drug samples obtained in the emergency department

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Objective: Acute recreational drug toxicity is a common presentation in the emergency department (ED). The true content of

recreational drugs and/or novel psychoactive substance (NPS) is often not known. Unused drugs are often found on an individual when they present. While analysis of these may not alter individual patient management, it can be useful in understanding the substances being used in the local area. This study analysed "drugs" obtained from patients presenting to the ED with acute recreational drug toxicity to determine the range of substances, including NPS, used locally.

Methods: Recreational drug samples were obtained from patients presenting to the ED of a busy inner city hospital over a month. The samples were handled as controlled drugs and transported by police to a Home Office-approved laboratory. Samples were initially categorised on their physical appearance (tablet, powder, liquid, herbal). Tablet samples were visually compared to an online database before being subjected to a Marquis test for the confirmation of contents; if inconclusive further qualitative analysis was performed using gas chromatography–mass spectroscopy (GC–MS). Liquid and powder samples were analysed using attenuated total reflectance fourier transform infrared spectroscopy; if necessary, further analysis was also undertaken using GC–MS. Herbal samples were identified only by visual inspection.

Results: A total of 66 (36 liquid, 24 powder, 4 tablet, and 2 herbal) samples were collected. Results of analysis were as follows: tablet samples: diazepam (n = 2), MDMA (n = 1), and sodium valproate (n = 1); powder samples: 4-methylmethcathinone (n = 10), 3,4-methylenedioxy-N-amphetamine (n = 4), methoxetamine (n = 3), amphetamine (n = 2), methamphetamine (n = 1), ketamine (n = 1), phenazepam (n = 1), and a combination of para-methoxy-N-methylamphetamine/alpha-pyrrolidinopentiophenone/4-fluoromethamphetamine/4-methylmethcathinone (n = 1). One powder contained no recreational drugs, NPS or active pharmaceutical compounds; liquid samples: gamma-butyrolactone (n = 24), alkyl nitrites (n = 4), gamma-hydroxybutyrate (n = 1), and methadone (n = 1). Six samples were identified as being either water or aqueous solution containing no pharmacologically active compounds. Herbal samples: both herbal samples were visually identified as cannabis.

Conclusion: This study demonstrates the use of a range of both classical recreational drugs and NPS. Development of a network of EDs collecting and analysing samples from different geographical regions may help in the understanding of the use and availability of substances from different areas.

158. Limited awareness and use of the novel psychoactive substance methiopropamine in men who have sex with men in South London nightclubs

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Objective: Methiopropamine is a thiophene ring-based structural analogue of methamphetamine. It has recently been detected in police and border seizures in the United Kingdom and across Europe. In addition, its use has been confirmed in analysis of pooled urine samples from street urinals in London, UK.[1] However, there is no data available on the awareness of methiopropamine as a recreational drug among drug users or on the prevalence of its use.

Methods: This questionnaire study was carried out in three gay-friendly night clubs in South East London, UK, across two weekends in July 2013. After verbal consent, basic demographic details (age, sex, and self-identified sexual orientation) and participant awareness of and use of methiopropamine and mephedrone were collected.

Results: Three hundred and ninety-seven participants completed the questionnaire: 89% were male, mean ± SD age was 30.1 ± 8.4 years, and 75% self-identified themselves as men who have sex with men (MSM). More participants had heard of mephedrone compared with methiopropamine (96.0%vs.13.9%, $p < 0.001$). Life-time use and last-month use of mephedrone were significantly higher than those of methiopropamine (life-time use: 76.6%vs.6.0%, $p < 0.001$; last-month use: 62.2%vs.1.5%, $p < 0.001$). There was no difference between MSM and non-MSM in terms of their awareness of methiopropamine or life-time/last-month use (awareness, 13.9%vs.13.8%; OR = 0.999; 95%CI, 0.520–1.921; p = 1.0; life-time use, 6.0% vs. 5.9%; OR = 1.025; 95% CI, 0.395–2.658, p = 1.00; last-month use, 1.4%vs.1%; OR = 0.678; 95% CI, 0.122–3.759, p = 0.647).

Conclusion: This study shows that there is limited awareness and self-reported use of methiopropamine in this population who have a high awareness and self-reported use of the established NPS mephedrone. Detection of methiopropamine in pooled urinal samples may reflect intended use by individuals, or unintentional use related to mis-selling of methiopropamine as an alternative recreational drug. Further work is needed to understand the true use of methiopropamine in larger population studies.

Reference

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159. K2—not the spice of life: Synthetic cannabinoids and ST elevation myocardial infarction: a case report

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Objective: The so-called designer drugs, including synthetic cannabinoids, have become prevalent and widely available. Synthetic cannabinoids are used as a substitute for marijuana but are not detected by routine urine toxicology immunoassays. The adverse effects of synthetic cannabinoids are not well-described nor have they been thoroughly studied.

Case report: A 16-year-old male with past medical history of asthma and attention deficit hyperactivity disorder (ADHD) presented to the emergency department (ED) complaining of 24 hours of non-radiating pressure-like substernal chest pain associated with dyspnea, nausea, and vomiting. He reported smoking cigarettes daily and occasional marijuana use, but denied recent use

of marijuana. The initial vital signs included a blood pressure of 127/57, heart rate of 82, respiratory rate of 22, oral temperature of 98.6°F, and pulse oximetry of 100% on room air. The initial electrocardiogram (EKG) revealed ST segment elevations in leads II, III, AVF, and V4, V5, V6. The initial troponin was 1.47 ng/mL (normal, 0–0.03 ng/mL) and the initial CKMB was 17.5 ng/mL (normal, 0–7 ng/mL). The patient eventually admitted to smoking "K2" 60–90 minutes prior to the onset of symptoms. In the ED, the patient received nitroglycerin, aspirin, and morphine, with mild improvement in symptoms. An echocardiogram revealed no pericardial effusion, normal myocardial function, and a structurally normal heart. The patient manifested persistent ST elevations with a peak troponin of 8.29 ng/mL and a peak CKMB of 33.9 ng/mL. The patient also had a urine drug immunoassay that was positive for benzodiazepines and opiates; of note, his urine was tested after receiving lorazepam and morphine during his hospital stay. On hospital day 4, cardiac catheterization revealed a subendocardial myocardial infarction due to coronary spasm with normal coronary arteries.

Conclusion: Synthetic cannabinoids are prevalent drugs of abuse with significant potential adverse effects. Chest pain is a very common presentation in adolescents; however, chest pain due to myocardial ischemia is exceedingly rare. When evaluating patients with chest pain, it is important to elicit a very detailed drug history, specifically asking about synthetic cannabinoids. Urine drug immunoassays are notoriously unreliable and in this case did not detect synthetic cannabinoids.

160. "WTF": A case of acute cerebral ischemia following synthetic cannabinoid inhalation

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Objective: Synthetic cannabinoid receptor agonists (SCRAs) are increasingly being used in the United States as marijuana substitutes. However, reports of severe toxicity resulting from their use are limited. This study presents a case of an acute cerebral ischemia following SCRA inhalation.

Case report: A 33-year-old man with no significant past medical history presented to the emergency room (ER) with right-sided weakness and aphasia. He had smoked two "joints" of a SCRA product labeled as "WTF" 10 minutes prior to the onset of his symptoms. His vital signs upon arrival were as follows: blood pressure, 163/63 mmHg; pulse, 100/min; respirations, 16/min; oxygen saturation, 99% on room air; and afebrile. Physical examination was significant for dense right hemiparesis, dysarthria, and aphasia. Basic laboratory evaluation, electrocardiogram (ECG), and head computed tomography(CT) were unremarkable. His repeat blood pressure had spontaneously normalized, so intravenous tPA was administered. Over the next 30 minutes, his National Institutes of Health (NIH) stroke scale improved from 5 to 3, and his symptoms continued to improve thereafter. A repeat head CT showed acute infarction in the left insular cortex. His hypercoagulability panel was normal, and the patient was discharged home neurologically intact after 3 days in the hospital. Urine toxicology results were positive for opiates and negative for cocaine, cannabinoids, methadone, barbiturates, and benzodiazepines. The "WTF" product was tested at the Center for Drug Detection and Response (Little Rock, Arkansas). Validated gas chromatography–mass spectrometry (GC–MS) results confirmed that the vegetable material contained in the "WTF" package had been laced with a SCRA known as XLR-11 or 1-(5-fluoropentyl)-1H-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl) methanone.

Conclusion: XLR-11 has previously been associated with acute kidney injury in humans.[1] However, there are no reports of it causing acute cerebral ischemic events. Since the patient presented here was young and had no cerebrovascular risk factors, the close temporal association between XLR-11 inhalation and his stroke is concerning. Acute cerebral infarction may occur after XLR-11 use in healthy patients.

Reference

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161. The electric koolaid NBOMe test: LC-TOF/MS confirmed 2C-C-NBOMe (25C) intoxication at Burning Man

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Objective: Designer drugs are constantly evolving, with the NBOMe derivatives of the 2C class of phenethylamines recently emerging in the European and United States drug markets. Cases of 2C-I-NBOMe toxicity have recently been reported in the literature. No reports to date describe the clinical effects 2C-C-NBOMe toxicity.

Case report: A 24 year-old female with no significant past medical history was screaming in her tent while camping in Black Rock City, NV, USA. She had profound agitated delirium after drinking wine, smoking marijuana, and ingesting 3 doses of what she thought was lysergic acid diethylamide (LSD, acid). She thought she was being attacked by invisible assailants and was not oriented to person, place, or time. Her physical examination was significant for tachycardia of 140 beats per minute, tachypnea of 32 respirations per minute, and mydriasis. Her skin was moist and hot to the touch. She was transported from her campsite to a clinic by emergency medical personnel, where she was treated with intravenous normal saline and lorazepam with complete recovery within 10 hours. Seven other people had ingested single doses from the same blotter paper that evening, but none had similar adverse effects. Leftover blotter paper samples were analyzed using Agilent Liquid Chromatograph-Time-of-Flight Mass Spectrometer (LC1200-TOF/MS 6230). Chromatograms obtained were analyzed using Agilent's 9000-compound Forensics

database in Agilent's MassHunter Qualitative Analysis software to determine the presence of drug(s). 2C-C-NBOMe was the primary compound detected, with a smaller amount of 2C-I-NBOMe also confirmed. We obtained a formula match to a dichlorinated version of 2C-C-NBOMe, but were unable to confirm its presence due to the lack of reference standards for that compound.
Conclusion: Using LC-TOF/MS, 2C-C-NBOMe was detected in blotter paper samples ingested by a patient with tachycardia and agitated delirium who had complete recovery. This is the first reported case of human 25C toxicity, raising concern about novel designer drugs of abuse mimicking delivery methods of older drugs such as LSD.

162. Acute agitation and chest pain from 5-fluoro-AKB48: A novel synthetic cannabinoid

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Objective: To describe a case of acute toxicity after inhalational exposure to 5-fluoro-AKB48, a novel synthetic cannabinoid.
Case report: A previously healthy 29-year-old male presented to the emergency department (ED) with chest pain and agitation. He bought and smoked a product by the name "Northern Lights Skunk – Pure Herbal Incense," which he believed to be a form of herbal marijuana. This was the first time he had smoked this product and denied co-ingestion of alcohol or other substances. Within minutes of smoking the product, the patient developed chest discomfort. On arrival in ED, he had a reduced Glasgow Coma Scale of 14 (E4, V4, M6); pupils, 5 mm, equal and reactive; blood pressure, 170/95; heart rate, 110; respiratory rate, 20; saturation, 100% on room air; and temperature, 36.5ºC. The patient was extremely agitated, unable to keep still, twitching and clutching his chest due to discomfort. Intravenous access was obtained and 4 mg midazolam administered intravenously (IV). He received a total of 2 litres of normal saline rehydration. For ongoing agitation, he required a further 1 mg of IV midazolam 1 hour later, followed by 5 mg of oral diazepam. He subsequently improved over a period of 2 hours and became alert and coherent. Electrolytes, full blood count, liver function tests, and serial cardiac enzymes were within normal limits. Electrocardiogram showed sinus rhythm with no ischaemic changes. Chest X-ray was unremarkable. After overnight observation and return to normal vital signs, the patient was discharged without complications. Follow up at 1 month was uneventful without return of any symptoms. The herbal product was analysed using nuclear magnetic resonance and mass spectroscopy. The main active compound was identified as 1-(5-fluoropentyl)-N-(tricyclo[3.3.1.13,7]dec-1-yl)-1H-indazole-3-carboxamide, otherwise known as 5-fluoro-AKB48, the 5-fluoro- analogue of AKB48 (APINACA). This synthetic cannabinoid, first identified in 2012 and named after the famous Japanese pop girl band, binds CB1 and CB2 receptors.
Conclusion: To our knowledge, this is the first reported case describing clinical toxicity from 5-fluoro-AKB48, a novel synthetic drug acting at cannabinoid receptors. Our patient experienced chest pain, tachycardia, hypertension, and agitation, all of which were self-limiting and required only benzodiazepines.

163. Synthetic cannabinoids: Impact of Australian legislation; is the problem Kronic or chronic?

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Objective: To describe the epidemiology of synthetic cannabinoid exposures reported to an Australian Poisons Information Centre, in order to monitor the impact of legislation by state and federal governments to restrict the sale of synthetic cannabinoids.
Methods:A retrospective review of calls made to our Poisons Information Centre during January 1,2010–November 9,2013 of reported exposures to synthetic cannabinoids based on patient history.
Results: One hundred and eighty cases were identified, with the incidence increasing from 28 in 2011 to 91 in 2013. Three-quarters were male and the median age was 19 years, IQR: 17–25. One hundred and forty-eight people (82%) needed hospitalization. There were 70 cases reported in the 5 months prior to new state-based legislation banning synthetic cannabinoids by brand name on June 9,2013.[1] The number of exposures reduced by 71% in the 5 months following the ban, with 20 cases reported. This contrasts with the effect of federal legislation from July 8,2011 banning 8 specific synthetic cannabinoids,[2] where a 50% increase in cases in the 5-month follow-up was observed (10 before vs. 15 after); and an all class ban from May 1 2012[3] where a 27% increase occurred (15 before vs. 19 after). The brand names of these products continue to diversify with many products now lacking a known brand (Table 1).
Conclusion: It appears that the 2013 legislation with its associated enforcement has been effective at reducing synthetic cannabinoid exposures in Australia covered by NSWPIC. However, ongoing usage associated with serious adverse effects is still occurring, warranting continued vigilance. An apparent effect of the bans appears to be a switch to generic non-branded products.

Table 1. Top brand names of synthetic cannabinoid exposures reported to NSW Poisons Information Centre (N = 180).

Brand name	Number
None	57
Kronic	39
Ash inferno	13
Black widow	13
Northern Lights	9
K2	8
Galaxy	3
Jungle fever	2
Red venom	2
Black mamba	2
Smoking hot	2
Vortex inferno	2
Others*	30

*30 different brands with one exposure each

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164. Death by spice: A case report of mortality following synthetic cannabinoid use

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Objective: Synthetic cannabinoids, more commonly known as "spice" or "K2", have been reported in the United States since the late 2000s. In 2011 alone, there were almost 7000 calls to US poison centers related to "spice", and calls remain prevalent to this day. Only one death has been reported from synthetic cannabinoids; the cause of death was a self-inflicted neck wound while intoxicated.[1] The objective of this report is to highlight the danger of a primary cardiac event following synthetic cannabinoid abuse.

Case report: A 49-year-old male was brought to the emergency department from home following resuscitation from an asystolic cardiac arrest after reportedly smoking "spice." Initial electrocardiogram (ECG) revealed ST elevation in aVL, V2, and V3 with reciprocal depression in II, III, aVF, and V4. A bedside echocardiogram demonstrated septal wall motion abnormality consistent with ischemic changes. A therapeutic hypothermia protocol was initiated, and he was taken directly to the cardiac catheterization laboratory where no significant atherosclerosis or coronary artery disease was found. On hospital day 3, ventilator and vasopressor support were withdrawn after brain death was suggested by an abnormal electroencephalogram. His troponin peaked at 0.21 ng/mL. Extensive drugs of abuse testing returned positive only for metabolites of synthetic cannabinoids: JWH-018 N-(5-hydroxypentyl), UR-144 N- (5-hydroxypentyl), and UR-144 N-pentanoic acid. A complete urine drug screen test, a hallucinogenic screen, and a sympathomimetic screen that included synthetic cathinones were all negative.

Discussion: To our knowledge, this marks the first case report of a primary cardiac event caused by synthetic cannabinoids leading to cardiac arrest and eventual death. The patient's troponin elevation, ST elevation, and wall motion abnormality in the setting of plaque free coronary arteries are highly suspicious for coronary artery vasospasm. The absence of other substances on extensive drug testing decreases the likelihood that other agents were contributing to the patient's presentation.

Conclusion: Health care providers should be aware of the potential for synthetic cannabinoids to cause a cardiac arrest.

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165. Exposure to 5f-P22, 5 IAI and diclazepam: A case report

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Objective: To report an exposure to 5f-P22, 2-aminoindane (5 IAI), and diclazepam in France in 2013.

Case report: A 34-year-old Caucasian male presented to our emergency department (ED) 1 hour after ingesting two pills sold on the Internet for "Laboratory reagent Use." Clinical examination showed an anxious patient, blood pressure (BP) was 135/73 mmHg, heart rate (HR) 110 bpm, and SpO_2 99%. Electrocardiograph (ECG) was normal. Temperature was 37°C. Dextrose was 6 mmol/L. Biology was unremarkable. He was discharged the same day. The first pill was green, in a bag, with a picture of the molecule and the formula: 7-chloro-5-(2-chlorophenyl)-1-methyl-1-1,3-dihydro-2H-1,4-benzodiazepin-2-one, diclazepam (chlorodiazepam).The other pill was rose-red, with a mention of the name: 2–3-dihydro-1H-inden-2-amine, CAS: 2975-41-9, sold as 5 IAI corresponding to 2-aminoindane which is an amphetamine. A week later, the same patient came to our ED again, 1hour after smoking a beige powder. After dizziness and drowsiness at home, the patient was alert with mydriasis; BP was 120/70 mmHg, HR 100 bpm, and SpO_2 99%. ECG was normal,and temperature was 36°C. Dextrose was 6.7 mmol/L. ECG was normal. Duration of signs was 3 hours. Mentioned on this new bag were as follows: quinolin-8-yl-(5-fluoropentyl)-1H-indole-3-carboxylate, CAS number: 14000742-41-7, name 5f-pb22, and a drawing of the molecular structure. It is a new synthetic cannabinoid of the JWH, CP, or AM series.

Discussion: Synthetic cannabinoids are used as herbal highs. Particular effects such as agitation, aggression, sweating, and logorrhoea are due to a stronger affinity for CB1 and CB2 receptors; tachycardia and mydriasis are usual. A few milligrams can induce clinical signs. Duration of effects is not well known except for tetrahydrocannabinol. Identification of these synthetic cannabinoids (powder or in blood samples) is difficult, needing a high-tech laboratory with nuclear magnetic resonance spectroscopy (NMR). Diclazepam is a benzodiazepine, not marketed as medication, estimated to be tenfold more active than diazepam. 5 IAI, synthesized in 1942 and used as stimulant drug since 2010, is well described in publications since 2013. These drugs (non-scheduled in France) are the subject of reports to French Pharmacodependance Centers and the Observatoire français des drogues et des toxicomanies (OFDT).

Conclusion: New drugs can induce particular clinical signs. Neurological signs may be more pronounced after synthetic cannabinoid exposure. New drugs are often sold for laboratory reagent use. Laboratory investigations are difficult.

166. Monoamine transporter and receptor interaction profiles of halogenated phenethylamines

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Objective: Novel halogenated amphetamines are increasingly available over the Internet and recreationally abused. The pharmacological mechanism of action of these designer drugs is largely unknown. We assessed the pharmacological activity profiles of a series of para-halogenated phenethylamines including cathinones *in vitro* and in comparison with known drugs of abuse.
Methods: We tested whether the novel compounds inhibit the norepinephrine (NE)-, dopamine (DA)-, and serotonin (5-HT) transporters (NET, DAT, and SERT, respectively) or release NE, DA, or 5-HT from monoamine-preloaded HEK293 cells containing the human transporters. Binding affinities at monoamine receptors were also assessed.
Results: Both the para-substituted phenethylamines 4-fluoroamphetamine (4-FA) and 4-fluoromethamphetamine (4-FMA) were potent NET inhibitors but differed in their ability to block the DAT and SERT. Both compounds exhibited profiles relatively similar to amphetamine or methamphetamine, but with twofold lower potency at NET and DAT, and twofold higher potency at SERT. Thus, para-fluoro-substitution enhanced the relative serotonergic activity. 4-Fluoroephedrine (4-FEP) inhibited NET with low potency but had no effects on the DAT and SERT. 4-Bromomethcathinone (4-BMC) showed a profile similar to its commonly abused cathinone analog mephedrone (4-methylmethcathinone), with a slightly higher potency as SERT inhibitor. Thus, para-bromo-substitution enhanced the serotonergic activity. 4-Ethylmethcathinone (4-EMC) was tenfold less potent at the NET and DAT, and equally potent at the SERT compared with mephedrone. Thus, similar to halogenation, para-ethylation reduced catecholaminergic activity while retaining serotonergic activity. Several of the novel drugs including 4-FA and 4-FMA also induced transporter-mediated release of preloaded neurotransmitter similar to the classic amphetamines.
Conclusion: The mode of action of the novel halogenated amphetamine derivatives is overall similar to that of the classic amphetamines. However, considerable pharmacological differences with regard to the relative activity of the drugs for the NET, DAT, and SERT exist, which likely influence clinical toxicity and abuse liability.

167. Prevalence of analytically confirmed intoxications by new psychotoxic substances in Italy: Data from Pavia Poison Centre and National Early Warning System

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Objective: Prevalence and the severity of patients admitted to the emergency departments (EDs) for new psychoactive and toxic substances (NPTS) are generally unknown, and in most cases, the standard toxicological screening gives negative results. The underestimation of this phenomenon could have direct implications on early diagnosis and clinical management. A study was conducted by the national EDs network referring to the Pavia Poison Centre (PPC) in order to evaluate the clinical features and the prevalence of analytically confirmed NPTS intoxications.
Methods: All consecutive cases referred to the PPC (Jan 2010-Aug 2013) for suspected/confirmed substances of abuse poisoning were evaluated (n = 5593); cases (n = 1723) presenting history for NPTS or atypical-clinical pictures after old/classical drug abuse were included. Cases were assessed for age, history, acute clinical manifestations, evolution, and toxico-analytical investigations. Cocaine, opiates, cannabis, and amphetamine/methamphetamine were defined as "old drugs". Ethanol intoxication and body-packers were excluded.
Results: Among 1723 cases of substance of abuse intoxication, 604 (35%) met the inclusion criteria. In 224/604 (37%) NPTS were declared; 30% of patients were unable to report the substances taken. The most common clinical manifestations were agitation (43%), tachycardia (35%), hallucinations (23%), mydriasis (21%), gastrointestinal discomfort (17%), drowsiness (17%), mental confusion (15%), coma (14%), seizures (5%), and hyperthermia (4%); 8 fatal cases were registered. Laboratory investigations were performed in 91% of cases; 82% of biological samples/products were delivered to PPC by courier (non-urgent analysis). The NPTS identified were MDMA (50 cases), ketamine (38), synthetic-cannabinoids (22), methoxetamine (17), caffeine (17), atropine-scopolamine (15), synthetic-cathinones (13), gamma-hydroxybutyric acid (GHB)/gamma-butyrolactone (GBL) (6), benzofurans (3), para-methoxyamphetamine (PMA)/para-methoxy-N-methylamphetamine (PMMA) (3), 2C-series (2), armine/dimethyltriyptamine (1).
Conclusion: The network of EDs referring to PPC and the support of advanced toxicological analyses are essential for the identification of NPTS-related poisonings; however, this cannot quantify the phenomenon. The clinico-toxicological evaluation of identified laboratory-confirmed NPTS intoxications permits regulatory actions by the Department for Antidrug Policies (DPA) and the Ministry of Health aimed at prevention and control, such as the inclusion of the NPTS in the list of controlled substances (excluding analogues, 22 new molecules has been controlled since 2010).
Acknowledgements: The study was carried out with the support of DPA—Presidency of the Council of Ministers.

168. Toxicity after reported use of "benzofury" compounds ([2-aminopropyl]-2,3-dihydrobenzofurans) compared with mephedrone: A report from the UK National Poisons Information Service

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Background: Recreational use of (2-aminopropyl)-2,3-dihydrobenzofurans "benzofury compounds" first emerged in the United Kingdom in 2010. The first enquiry to the UK National Poisons Information Service (NPIS) was received in July 2010, shortly after legal control of mephedrone in the United Kingdom in April 2010.[1]
Objective: This study was conducted to compare the demographics and toxicity reported following exposure to benzofury compounds and mephedrone, using data collected routinely by NPIS.
Methods: NPIS patient-specific telephone enquiries and user sessions for TOXBASE®, the NPIS online information database, relating to benzofury compounds and mephedrone (ingestion only) were reviewed from March 2009 to April 2013. Cases involving co-ingestion of other substances (apart from alcohol) were excluded from the comparison.
Results: There were 64 telephone enquiries and 741 TOXBASE user sessions regarding benzofury compounds during the period of study; most enquiries were received in August 2010 (33 calls, 112 TOXBASE sessions). All use was by ingestion; in 9 patients other substances were also involved (5-iodo-2-aminoindane (5-IAI), etizolam, dimethocaine, mephedrone, and 5,6-methylenedioxy-2-aminoindane (MDAI), alpha methyltryptamine, olanzapine, and sildenafil). The remaining 55 cases were compared with 304 patients using mephedrone alone by ingestion. Stimulant features such as tachycardia, hypertension, mydriasis, palpitation, fever, increased sweating, and tremor (72.7% vs. 38.8%; odds ratio [OR] 4.2; 95% confidence intervals [CI], 2.22–7.95, P = 0.0001) and mental health disturbances (60% vs. 37.5%; OR, 2.5; 95% CI, 1.39–4.50, P = 0.0027) were significantly more common after use of benzofury compounds. The WHO/IPCS/EC/EAPCCT Poisoning Severity Scores (PSS)[2] of moderate or severe were recorded more frequently in benzofury users (45% vs.16%; OR, 4.44; CI, 2.41–8.21, P = 0.0001). No fatalities were reported to NPIS following benzofury exposure, compared with 2 deaths for oral mephedrone (P = NS).
Conclusion: Stimulant effects, mental health disturbances, and PSS of moderate or severe are more commonly reported in NPIS enquiries involving benzofury compounds than after oral use of mephedrone.

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169. Patterns of presentation and clinical toxicity after reported intravenous use of mephedrone in the United Kingdom. A report from the UK National Poisons Information Service

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Background: The use of mephedrone, a synthetic cathinone with amfetamine-like properties, first emerged on the UK recreational drug scene in 2009 and it grew rapidly[1], although the number of cases reported to the NPIS fell substantially after the drug was subject to legal control in April 2010.[2,3] Recently, concerns have been raised about an apparent increase in the use of intravenous (IV) mephedrone, sometimes termed "M-Smack."[4]
Objective: This study was performed to determine the toxicity of IV mephedrone in comparison with mephedrone use via other routes.
Methods: UK National Poisons Information Service (NPIS) telephone enquiries related to mephedrone were reviewed from March 2009 to September 2013.
Results: Of 786 enquiries regarding mephedrone, 20 (2.5%) related to IV exposure, with the first IV case reported in February 2010. Thereafter, NPIS received 4 calls in 2010, 4 in 2011, 7 in 2012, and 4 in the first 9 months of 2013. Compared with other routes, IV users were more likely to be male (90% vs. 69%, P = 0.048) and their median age was older (30y vs. 21y). There were no significant differences in reported features comparing IV use with other routes, including stimulant effects (e.g., tachycardia, hypertension, mydriasis, [40% IV vs. 39% other routes]), agitation (30% vs. 22%), tachycardia (30% vs. 22%), fever (15% vs. 4%), raised creatine kinase (15% vs. 6%), hallucinations (10% vs. 4%), convulsions (0% vs. 3.5%), and death (0% vs. 0.4%).
Conclusion: IV use of mephedrone is reported uncommonly to the NPIS. No differences in the toxicity of IV mephedrone compared to other routes were identified, but the sample size was small.

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170. Patterns of presentation and clinical toxicity after reported use of alpha methyltryptamine in the United Kingdom: A report from the UK National Poisons Information Service

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Background: Alpha methyltryptamine (AMT) is an indole analogue of amphetamine that acts by increasing the release and inhibiting the reuptake of dopamine, noradrenaline, and serotonin and by inhibiting monoamine oxidase. It has been used recreationally for its hallucinogenic properties for many years, but has been encountered only rarely in the United Kingdom.[1]
Objective: This study was performed to characterize the pattern of acute toxicity following recreational use of AMT, as reported by health professionals to the UK National Poisons Information Service (NPIS).
Methods: NPIS telephone enquiries were reviewed from March 2009 to September 2013, and user sessions for TOXBASE®, the NPIS online information database, were from January to September 2013. Telephone enquiry data were compared with those for mephedrone (ingestion and insufflation only).
Results: There were 63 telephone enquiries regarding AMT during the period of study, with no telephone enquiries in 2009 or 2010, 19 in 2011, 35 in 2012, and 9 in 2013. Most patients were male (68%) with a median age of 20 years. The route of exposure was ingestion in 55, insufflation in 4, and unknown in 4 cases. Features reported more frequently in AMT compared with mephedrone users (n = 704) included acute mental health disturbances (67% vs. 35%; odds ratio [OR], 3.77; 95% CI, 2.18–6.51), stimulant effects (tachycardia, hypertension, mydriasis, palpitation, fever, increased sweating, and tremor [62% vs. 38%; OR, 2.66; 95% CI, 1.56–4.52], reduced consciousness (16% vs. 8%; OR, 2.14; 95% CI, 1.03–4.44), and seizures (14% vs. 3%; OR, 4.72; 95% CI, 2.10–10.67). The WHO/IPCS/EC/EAPCCT Poisoning Severity Scores[2] of 2 (moderate) or 3 (severe), both current at the time of the enquiry and maximum, were recorded more frequently in users of AMT than in the users of mephedrone.
Conclusion: Although still uncommon, toxicity following exposure to AMT has been reported more frequently in the UK since 2011. Mental health disturbances, stimulant features, reduced conscious level, and seizures are all reported more frequently in those presenting following reported use of AMT than mephedrone.

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171. Very low-dose naltrexone versus placebo in alleviating withdrawal manifestation

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Background: Reducing the symptoms of withdrawal syndrome and completing the treatment are the initial focus of opioid detoxification.[1] Very low-dose naltrexone (VLNTX) was recently found to reduce opioid tolerance and dependence in animal and human clinical study therapies.[2,3] This study focused on evaluating safety and efficacy of VLNTX in reducing withdrawal symptoms during detoxification.
Methods: In a double-blind randomized control trial (IRCT 2013081914404N1), 64 opioid-dependent subjects who were referred for abstinence therapy were included. Subjects were divided into two groups and received VLNTX 0.125 mg or placebo daily for 10 days, together with the routine clonidine-based protocol. The severity of withdrawal symptoms was assessed on the 1st and 10th day of treatment.
Results: In total, the majority of reported clinical manifestations on the 1st day significantly reduced in both groups. During the whole 10 days of follow-up, runny eyes ($p = 0.006$), anxiety ($p = 0.031$), and dehydration ($p = 0.014$) were significantly reduced in the 0.125-mg group of VLNTX-treated individuals. Craving ($p = 0.016$) and calf pain ($p = 0.027$), however, were significantly higher in this group. No further differences were found. On the 10th day there was not any significant difference between 0.125 mg and placebo groups.
Conclusion: Based on this study, VLNTX could reduce some withdrawal symptoms in the starting days of detoxification. In the next few days, the difference between VLTNX and placebo will wear off. Further studies are needed to test the utility of this new therapeutic approach.

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172. Assessing the validity of capillary dried blood spots used for gamma-hydroxybutyrate analysis from patients suspected of toxicity attending the emergency department

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Objective: Recreational gamma-hydroxybutyrate (GHB) use can cause significant, potentially life-threatening acute toxicity. Currently, venous blood is the gold standard biological matrix for analysis. Dried blood spots (DBS) offer a more versatile alternative to venous blood; however, their use in the measurement of GHB concentrations has not been validated in a clinical context. The objective of this prospective cohort study was to investigate use of capillary DBS (cDBS) against the venous blood GHB concentration.
Methods: Consecutive patients admitted to our emergency department with suspected GHB toxicity had paired cDBS and venous blood samples taken on arrival. cDBS were taken by finger prick with blood dropped onto a filter paper, air-dried, and stored with desiccant in a zip closure bag at room temperature. Whole blood was taken in fluoride/oxalate tubes to prevent enzymatic degradation and stored at -20°C. cDBS and venous blood GHB analysis was conducted using methods described previously.[1,2] Samples were analysed only if patients consented retrospectively. The study was approved by the National Research Ethics Committee (IRB).
Results: Fifteen patients (14 male, 30 ± 9 years) consented—at admission all had clinical features of GHB toxicity (median GCS, 7; range, 3–14). Mean± SD venous blood and cDBS GHB concentrations were 160.5 ± 113 µg/mL and 169.9 ± 123 µg/mL, respectively. Bland–Altman analysis demonstrated a mean difference between the 2 measures of 9.42 µg/mL (limitation of agreement, −22.5–41.3). Two-way random effects model for intraclass correlation coefficient was 0.988 (95% CI, 0.956–0.996, $p < 0.001$).
Conclusion: This study shows strong agreement between venous and cDBS GHB concentrations, although the cDBS slightly overestimates GHB concentrations. cDBS offers numerous advantages (e.g., ease of collection, reduced infection risk, and sample stability) over venous blood. Further validation is required in a larger patient cohort before accepting cDBS as the sampling modality of choice for GHB analysis.

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173. Drug analysis and clinical effects in patients attending the emergency department with suspected gamma-hydroxybutyrate toxicity

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Objective: Recreational gamma-hydroxybutyrate (GHB) use can cause significant toxicity, in particular coma and respiratory depression. However, there are limited data on the relationship between clinical features of GHB toxicity and GHB concentrations. The objective of this prospective cohort study was to investigate this relationship.
Methods: Consecutive patients presenting to an inner-city emergency department (ED) with suspected GHB toxicity had a venous blood sample taken on arrival (in fluoride/oxylate tubes to prevent enzymatic degradation). Half of the sample was centrifuged at 3000 g for 10 minutes, and the plasma was removed for comprehensive recreational drug analysis using ultra-performance liquid-chromatography with time-of-flight mass-spectrometry. Venous whole blood was used for GHB analysis using gas-chromatography–mass spectrometry. Data on presenting clinical features were collected on all patients. The study was approved by the National Research Ethics Committee (IRB).
Results: Fifteen patients (14 male, 30 ± 9 years) were recruited, and GHB was analytically confirmed in all patients (mean concentration, 160.5 ± 113 µg/mL; range, 84–526 µg/mL). No additional recreational drugs/ethanol were found in two patients. Only two patients had ethanol detected (0.27 and 1.1 g/L; ethanol was the only other substance detected in the latter case) One or more other recreational drugs were detected in 12 patients: mephedrone ($n = 12$), methamphetamine (5), ketamine (4), 4-methylethcathinone (2), amphetamine (1), and benzodiazepines (1). At presentation, clinical variables included were as follows: heart rate, 65 ± 17 (range, 45–102) bpm; systolic blood pressure, 124 ± 19 (range, 93–169) mmHg; respiratory rate 15 ± 4 (5–21) per minute, $paCO_2$ 6.42 ± 0.95 (5.12–8.31) kPa, temperature 35 ± 0.64 (34.5–35.4) ˚C, pupil size 3.6 ± 2 (2–8) mm, and Glasgow coma scale (GCS) of 7 ± 3 (3–9). All patients with venous GHB concentrations of > 200 µg/mL ($n = 3$, 20%) had a GCS of 3/15 and required intubation. Using linear regression analysis of the clinical parameters, venous GHB concentrations could be predicted by the presence of an increased $paCO_2$ ($R^2 = 0.61$, $p = 0.02$) and a reduced GCS ($R^2 = 0.35$, $p = 0.02$).
Conclusion: Patients admitted to the ED with GHB toxicity have a distinctive toxidrome that appears to correlate with systemic GHB concentrations at the time of assessment. The majority of the patients with GHB toxicity had other recreational drugs detected on comprehensive toxicological analysis, although the clinical effects of these other drugs were not apparent. The results of this study need confirmation in a larger patient cohort.

174. What to do when they're stuffed?

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Objective: Body stuffers swallow or conceal illicit drugs to avoid detection by the police. These individuals can be at risk of drug toxicity if the drugs are absorbed. This study looked at the clinical course of body stuffers in order to determine the required period of observation in these patients.
Methods: A purpose-designed toxicological database was retrospectively interrogated to identify patients who were classified as "body stuffers" (defined as any person who ingested an illicit drug in order to escape detection by authorities and not for recreational purposes or for transportation across borders) presenting to our large inner-city emergency department January 1,2006–October 31,2011. Basic demographic data, drug(s) ingested, packaging, and clinical course were extracted from the database.
Results: One hundred and thirty-nine patients presented as body stuffers during the study period. One hundred and eighteen (85%) were male and 21 (15%) female. Mean age was 30.4 ± 8.1 years. Drugs involved were cocaine (n = 41, 30%), heroin (40, 29%), cocaine and heroin (21, 15%), other drugs (21, 15%), and unknown (16, 11%). Types of wrapping used were plastic bag (n = 30, 20.9%), cling film (26, 18.7%), cigarette paper (3, 2.2%), aluminium foil (2, 1.4%), condom (1, 0.7%), unwrapped (14, 10%), and unknown (61, 43.9%). The mean time from ingestion to time of presentation was 142.1 ± 190.2 minutes (range, 30–1560). Thirty-nine patients (28%) were asymptomatic, 91(65%) had features of acute drug toxicity at the time of presentation and 9 (6%) had other features not related to acute drug toxicity. One hundred and twenty-seven patients (91%) did not deteriorate or develop new features of acute drug toxicity. In the 12 patients (9%) who did develop new or worsening features of acute drug toxicity, all manifested within 6 hours of presentation (< 2 hrs, n = 4; 2–4 hrs, n = 5; 4–6 hrs, n = 3). Of these patients, 6 (50%) ingested heroin alone; 4 (33%), heroin and cocaine; 1 (8%), cocaine; and 1 (8%), unknown; 5 (42%) drugs were wrapped in cling film, 3 (25%) in a plastic bag, 1 (8%) in cigarette paper, and 3 (25%) were unknown.
Conclusion: Body stuffers who developed clinical features of acute drug toxicity did so within 6 hours of hospital presentation. We therefore propose that body stuffers can be managed with 6 hours of observation.

175. How common is injection drug use ("slamming") among men who have sex with men attending night-time economy venues?

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Objective: There is increasing concern about the injection ("slamming") of recreational drugs and novel psychoactive substances, particularly in men who have sex with men (MSM) communities. There are anecdotal reports from UK treatment services of increasing rates of injection of drugs such as mephedrone. However, these reports are from individuals with problematic drug use seeking specialist treatment, and may not be representative of the wider MSM community and/or of drug use in a recreational context in the night-time economy. This study was undertaken to understand the prevalence of injecting drug use among the MSM community attending night-time economy venues.
Methods: A questionnaire survey was carried out in three gay-friendly night-clubs in South East London, UK, over two weekends in July 2013. Participants gave verbal consent for inclusion. Basic demographic data were collected (age, sex, and self-identified sexual orientation) together with information on whether the individual had previously injected recreational drugs and if so, which drugs they had injected.
Results: Three hundred and ninety-seven participants completed the survey. Of these, 89% were male, mean ± SD age was 30.1 ± 8.4 years, and 75% identified themselves as MSM. Nineteen participants (5%) admitted to having ever injected drugs; there was no difference in the proportion of MSM and non-MSM who had previously injected drugs (5.4%vs.3.0%; OR = 1.8; 95% CI, 0.538–6.621, p = 0.42). Of these, the majority (n = 13) had previously injected only one drug, and only two participants had injected multiple drugs. Mephedrone was the most popular injected drug (n = 8); other injected drugs included "crystal methamphetamine" (n = 4), cocaine (n = 3), "speed" (n = 2), heroin (n = 1), and anabolic steroids (n = 1). Four participants did not specify which drug(s) they had injected.
Conclusion: This study shows that injection of recreational drugs and NPS is low in people who attend gay-friendly night clubs in South East London. Among the small minority who do inject recreational drugs, the most commonly injected drug was mephedrone. It is important that messages regarding the prevalence of injection drug use are accurate to enable appropriate targeting of resources to reduce the harms associated with this pattern of drug use.

176. A survey to establish current European data collection on emergency room presentations with acute recreational drug toxicity

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Objective: The European Drug Emergencies Network (Euro-DEN) is a European Commission funded project to improve the knowledge of acute recreational drug toxicity and assess the risks associated with new psychoactive substances (NPS). As a baseline for this project, we performed a survey to determine what sys-

tematic data are currently being collected and reported nationally in Europe on emergency room presentations with acute toxicity related to classical recreational drugs and NPS.
Methods: A SurveyMonkey® questionnaire was distributed in July 2013 to the nominated experts for the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) 30 national reporting Focal Points. The survey collected information on whether there was systematic data collection on emergency room presentations with acute toxicity related to classical recreational drugs and/or NPS at a national or regional level, and what kind of data and how the data were collected.
Results: There were 36 complete responses from 28 countries. At a national level, 10 countries (36%) collected information on NPS (hospital diagnoses [4], pre-hospital data [1], forensic data [2], poisons center data [5]); and 12 countries (43%) on classical recreational drugs; 15 countries (54%) did not have any national systematic data collection for either classical recreational drugs or NPS. At a regional level, 6 countries (21%) collected data on NPS; 8 (29%) on classical recreational drugs; 16 (57%) had no such collection; and 3 did not answer (11%). For NPS, basic demographics (12), drug names (12), clinical symptoms (10), and management (9) were the most commonly collected data on both levels. Outcome (7) and laboratory confirmation on NPS involved (4) were rarely collected.
Conclusion: The majority of European countries do not systematically collect or report data on emergency room presentations with acute recreational drug and NPS toxicity at either a national or a regional level. Particularly concerning is that only about one-third of countries collected any information on acute NPS toxicity. This is a rapidly evolving area, and there is a clear need for toxico-surveillance across Europe to inform the public health and legislative response. Data collected in the Euro-DEN project will help to close this knowledge gap.

177. Risk/degree of social exclusion that drug users are facing

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Objective: To assess the degree of social exclusion among problematic drug users who are not listed as beneficiaries of assistance services provided by the public or private system.
Methods: A simple random selection using the following criteria for inclusion: drug user over the past 12 months, age group 18–49 years, mental and physical ability to understand questions and directions, written consent in order to participate to this survey, to have lived in Bucharest for at least 6 months out of the 12 months prior to the date of the interview. Data collection used a specifically prepared questionnaire.
Results: Out of the 400 drug users from Bucharest included in the survey, 74.2% were men and 25.8% were women; 95% being born in urban area. Two variables were defined: the age and the marital status. Most of the respondents were occasional users (57%), the main drug used was cannabis (52.5%), and the main route of administration was smoking/inhalation (54.5%); 4.5% of respondents did not have identity documents, which caused a high risk of social marginalization by limiting their access to the basic services needed by every citizen. Only 21.4% of respondents believed that they were in a difficult situation because of drug use, most mentioned that problems were lack of money (41.9%) and of family support (23.9%). Lack of education and training was not perceived as a difficulty by those who participated in this survey, only 6% considering this as the reason for which they were excluded from society. In terms of occupational status, drug users in Bucharest were either employed with a labor contract with indefinite duration (33.6%), or unemployed or staying at home (38.5%). About a third (31%) of those included in the sample stated that they were not registered with a family doctor. 61.2% of the respondents said that their education level was sufficient for what they wanted to do in life, while 0.5% considered the level of training they had obtained was higher than their professional aspirations.
Conclusion: The risk of social exclusion among problematic drug users does exist but it is not well understood by them.

178. Drug consumption among patients admitted to a methadone maintenance program

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Objective: The aim of the study was to evaluate consumption of drugs of abuse (DOA) in subjects admitted to the methadone maintenance program (MMP). Seventy subjects (53 men, 17 women) were included in the study. The results were correlated with gender, age, and the job situation of the subjects. To the best of our knowledge, such studies are very rare;[1] the results may help MMP decision-makers and physicians to get a better overview of the current situation in DOA consumption of the patients.
Methods: The urine samples collected from the 70 subjects were part of routine drug analysis. The routine tests include alcohol, benzodiazepines, amphetamines, cannabinoids, cocaine, and opiates using immunoassay. These tests were completed by a general unknown screening with gas chromatography–mass spectrometry (GC-MS) and a liquid chromatography–tandem mass spectrometry (LC–MS/MS) screening for monitoring certain low-dosage opioids.
Results: In 19 (27.1%) subjects, no DOA was detected; in 30 subjects (42.9%), cannabis or cocaine or opiates were detected; and in 21 subjects (30%), two or three different DOAs were detected. No sample contained amphetamines or low-dosage opioids (e.g. fentanyl), and the presence of methadone was confirmed in all samples. Our results show that (i) the prevalence of the cocaine, cannabinoid, and opiate use is decreasing with the age of the patients, (ii) fewer drugs of abuse were detected in subjects having a job than in subjects not having a job, and (iii) fewer drugs of abuse were detected in female subjects then in male subjects. No drugs of abuse were detected in 47.1% of the female subjects compared to 20.8% of the male subjects.
Conclusion: Drug and poly-drug use is widespread in subjects admitted to MMPs. In particular, more than 40% of the patients were consuming heroin despite methadone treatment. Differences exist between men and women, younger and older subjects, and subjects with or without a job.

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179. Global Toxicosurveillance Network (GTNet): Characterizing prescription opioid exposures reported to European Poison Centres

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Objective: To describe patient and exposure characteristics for prescription opioids reported to poison centers (PC) in Göttingen, Germany; Milan, Italy; Netherlands; Switzerland; and the United Kingdom (UK).
Methods: Analyses include case characteristics by country for exposures reported in 2012 for buprenorphine, methadone, and oxycodone. Comparisons include age, gender, exposure reason, route, and drug. The analysis for exposure reason excludes The Netherlands as they began reporting exposure reason in 2013. Exposure reasons consisted of intentional (suicide), intentional (misuse, abuse, or diversion), and unintentional. Routes are categorized by oral or non-oral. Significant p-values indicate country differences in the distribution of the variable.
Results: There was no difference in gender ($p = .7740$) or age ($p = .1225$) across countries. There was a significant difference across countries for exposure reason ($p < 0.0001$), route ($p < 0.0001$), and drug ($p < 0.0001$). Mean age for all PCs was 39.8 (SD = 18.9) years, 58% were male. In all countries, there were more calls for exposures in males and the mean age was approximately 40 years. Buprenorphine had the lowest per cent of calls in all countries; however, drug availability may also vary across countries. The route (oral vs. non-oral) was significantly different across countries.
Conclusion: While the PC methods vary between countries, the case characteristics of exposures to oxycodone, buprenorphine, and methadone as reported to poison centers within European countries are not different. However, the drug the patient was exposed to, the route, and the reason were statistically significantly different by country.

180. Prescription opioid misuse in Europe: From opioid treatment programs to Poison Centres

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Objective: To describe prescription opioid misuse in Germany and Italy reported by patients entering opioid treatment programs (OTP) in Munich and Piemonte, Puglia, and calls to poison centres (PC) in Göttingen and Milan.
Methods: For PCs, analyses include intentional exposures reported in 2012 for buprenorphine, methadone, and oxycodone. For OTPs, data include self-reports of drug use "to get high" by patients entering opioid addiction therapy from January 2012 to August 2013 for buprenorphine, methadone, oxycodone, codeine, fentanyl, morphine, and tramadol. As the focus is on prescription drug misuse, heroin was excluded.
Results: In Germany, 70% of PC calls were intentional exposures. Mean age was 43.1 (SD = 16.0), 59% were male. Majority (87%) of intentional exposures involved oral route. Majority (57%) were suicidal intent. Forty-six per cent involved methadone, 36% oxycodone, and 18% buprenorphine. Of the 158 patients from OTP, 37% reported a prescription opioid as their primary drug used to get high, including methadone (39%) and buprenorphine (29%). Patients surveyed were 60% male with mean age of 36.6 (SD = 9.8) years. Injection of ≥ 1 drug in the past 30 days was reported by 81%, and 86% had previously been in treatment. In Italy, 77% of PC calls were intentional exposures. Mean age was 40.1 (SD = 15.1) years, 56% male. Majority (93%) of intentional exposures involved oral route. Of intentional exposures, 51% were for misuse and 49% were for suicide. Fifty-one per cent were for methadone, 34% for oxycodone, and 15% for buprenorphine. Of the 309 patients from OTP, 36% reported prescription opioid as their primary drug used to get high, including buprenorphine (43%) and methadone (32%). Patients surveyed were 69% male with mean age of 28.6 (SD = 8.2) years. Injection of ≥ 1 drug the past 30 days was reported by 18%, and 49% had previously been in treatment.
Conclusion: Data from PCs and OTPs in Germany and Italy illustrate similar pictures of prescription opioid misuse within each country. Drugs typically used to treat opioid addiction are among those most misused. Germany had a high rate of injection in OTPs as well as a high percentage of patients who had previously been in treatment.

181. What is the evidence of the misuse of sildenafil (Viagra) in UK men who have sex with men clubbers?

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Objective: There is anecdotal evidence of misuse of erectile dysfunction medication, particularly to counteract some of the unwanted effects of recreational drugs on erectile function. The

aim of this study was to evaluate the prevalence of sildenafil misuse in a UK population who have previously been shown to have a high prevalence of recreational drugs use.
Methods: We conducted a questionnaire survey of English-speaking adults who attended nightclubs that cater for the men who have sex with men (MSM) community in South London in June 2013. In addition to basic demographic data (age, sex, whether they had sex with men, women or both), data were collected on whether individuals had heard of sildenafil and if so whether they had ever used it without medical advice/prescription (non-medical use). Study participants were grouped as MSM if they were male and had sex either with men only or with both men and women.
Results: There were 313 respondents: 282 (90.1%) male, 30 (9.6%) female, and 1 (0.3%) transgender; mean ± SD age, 31.3 ± 7.6 years. Two hundred and forty-eight (79.2%) were MSM and 32 (11.3%) were non-MSM. One hundred and thirty-six (49.1%) MSM clubbers versus 6 (18.8%) non-MSM misused sildenafil in the last year ($p = < 0.001$). Among MSM, 232 (93.5%) had heard of sildenafil and 161 (64.9%) reported non-medical use in their lifetime. Last year and last month reported non-medical use rates were 133 (53.6%) and 93 (37.5%), respectively. The most common source was from friends 87 (54%). Other sources included: dealers 41 (25.5%); primary-care doctors 30 (18.6%); Internet suppliers 30 (18.6%); overseas sources 18 (11.2%); and family 7 (4.3%). Last-year recreational drug use was high in MSM who misused sildenafil: mephedrone, 92.5%; cocaine, 82.0%; gamma-hydroxybutyric acid (GHB)/gamma-butyrolactone (GBL), 74.4%; and MDMA, 74.4%.
Conclusion: This study demonstrates a high prevalence of non-medical use sildenafil in a group of clubbers who are heavy users of recreational drugs; it is not likely that this young population have underlying erectile dysfunction as a reason for legitimate use of sildenafil. There is the potential for interaction with other recreational drugs used including cocaine and volatile nitrites (e.g., poppers). Further work is required to determine whether this is a more widespread issue, to understand the reasons for non-medical use, and to study the prevalence of non-medical use of other longer-acting erectile dysfunction medications.

182. What is the evidence of the misuse of benzodiazepines and the "Z drugs" in UK men who have sex with men clubbers?

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Objective: Benzodiazepines and the "Z-drugs" (zopiclone, zaleplon, zolpidem) are commonly prescribed for anxiety, stress, and sleep disorders and have potential for misuse/dependence. This study evaluated the prevalence of non-medical use of these drugs in a UK men who have sex with men (MSM) clubbing cohort.
Methods: Adults attending nightclubs catering for MSM in South London were surveyed in June 2013. Basic demographic data (age, sex, whether they had sex with men, women or both) were collected, together with data on whether individuals had heard of a range of benzodiazepines and "Z-drugs" and if they had ever misused them. Participants were classified as MSM if they were male and had sex with men or both men and women.

Table 1. Percentage of MSM who had heard of/misused the drugs.

Drug Name	Number (%) of MSM respondents who had heard of the drug(s)	Number (%) of MSM respondents who had heard and misused the drug(s)
Diazepam (Valium)	196 (79.0%)	71 (36.2%)
Alprazolam (Xanax)	110 (44.4%)	26 (23.6%)
Nitrazepam	63 (25.4%)	10 (15.9%)
Lorazepam/lormetazepam/Ativan	61 (24.6%)	11 (18.0%)
Phenazepam	30 (12.1%)	6 (20%)
"Z-Drugs" (zolpidem/zopiclone/zaleplon)	87 (35.1%)	45 (51.7%)

Results: There were 313 respondents: 282 (90.1%) male, 30 (9.6%) female, 1 (0.3%) transgender; mean ± SD age, 31.3 ± 7.6 years. Two hundred and forty-eight (79.2%) were MSM, with high last month use of recreational drugs: 67.3%, mephedrone; 50.4%, GHB/GBL; and 42.3%, cocaine. Ninety-one (36.7%) MSM versus 4 (12.5%) non-MSM misused one or more of the benzodiazepines and "Z-drugs" in their lifetime ($p = 0.005$). Table 1 shows the percentage of MSM who had heard of/misused the drugs. Forty-two (46.2%) obtained these drugs from friends; 28 (30.8%) from dealers; 26 (28.6%) from a primary-care doctor; 21 (23.1%) from the Internet; 12 (13.2%) from overseas; and 8 (8.8%) from family.
Conclusion: This study shows a high prevalence of non-medical use of benzodiazepine and "Z-drugs" in this MSM clubbing cohort. Further work is needed to understand the reasons for the misuse and determine whether this is more widespread, inform public health initiatives to reduce non-medical use, and review whether tighter regulation is required.

183. Sudden sensorineural hearing loss after methadone overdose: A case series

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Objective: We present a rare but literature-described symptom in methadone overdose: sudden sensorineural hearing loss.
Case series: 1. A 36-year-old male, in substitution therapy with 60 mg/day of methadone for 3 years was admitted 12 hours after voluntary intravenous administration of 160 mg methadone with altered mental status, bilateral hearing loss, tachycardia, swelling, and oedema at the puncture site. Toxicological urine gas chromatography/mass spectrometry (GS/MS) testing: methadone. Audiometry testing performed at 24 hours: loss of -36 dB right ear and -52 dB left ear. The hearing loss completely resolved within 4 days. 2. A 24-year-old male, HIV and HCV positive, with a history of heroin abuse was admitted 3 hours after he voluntarily ingested 120 mg methadone as a suicide attempt; he needed ventilatory support, with pulmonary edema, miosis, tachycardia, and hypotension. Toxicological urine GS/MS testing: methadone. After 2 days, the general status improved: the patient was conscious, was weaned from ventilator support, but he claimed bilateral deafness. Audiometry testing performed at 52 hours: loss of -58 dB right ear

and -50 dB left ear. The hearing loss completely resolved within 8 days. 3. A 28-year-old woman, with a history of multiple drug abuse, in substitution therapy with methadone 40 mg/day for 2 years, was admitted 3 hours after ingestion of 80 mg methadone for recreational aim. She presented altered mental status, miosis, but was respiratory and hemodynamically stable. After 6 hours she was awake, but claiming hearing loss. Toxicological urine GS/MS testing: methadone. Audiometry testing at 16 hours: loss of -34 dB right ear and -48 dB left ear. After 2 days from ingestion, the hearing loss resolved completely.

Conclusion: In literature, cases of sudden sensorineural hearing loss related to methadone overdose have been reported, but the ototoxicity mechanism is unknown as yet. All 3 patients were without auditory troubles prior to admission, the methadone used was manufactured in a controlled environment (without contaminants), and the recovery was full and without sequelae. Methadone was the only drug identified in toxicological screening, and we suggest that methadone overdose is the cause of sudden sensorineural hearing loss.

184. A case of MDMA-associated rhabdomyolysis, disseminated intravascular coagulation, intracerebral hemorrhage, and multi-organ system failure potentially enhanced by propofol

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Objective: N-3,4-Methylenedioxymethamphetamine (MDMA) is an amphetamine derivative abused among young partygoers. Most of the observed morbidity and mortality is attributed to complications of hyperthermia. We report a rare case of MDMA exposure resulting in rhabdomyolysis, disseminated intravascular coagulation (DIC), intracerebral hemorrhage, and multi-organ system failure. An unexpected resurgence of transaminitis and rhabdomyolysis was associated with the initiation of propofol.

Case report: A previously healthy 21-year-old man developed altered mental status, rigidity, and diaphoresis several hours after ingesting a single MDMA pill ("Molly"). In the emergency department, he was febrile (109F), tachycardic (190 bpm), hypertensive (218/168 mmHg), with Glasgow coma scale (GCS) of 3, requiring intubation, paralysis, sedation, and active cooling. Within 48 hours, he developed rhabdomyolysis (creatine phosphokinase [CPK], 51050 U/L), fulminant hepatic failure (AST, 4885 U/L; ALT, 3128 U/L; INR, 3.7; grade IV encephalopathy; and T. bili 4377 μmol/L), renal failure (creatinine 489 μmol/L), and DIC (D-dimer > 20 μg/mL FEU, platelets $20x10^9$/L). Computed tomography of the brain revealed multiple intracerebral hemorrhages. Treatment included hemodialysis, N-acetylcysteine, and transfer to our liver transplant center on day 3. There was a marked unexpected resurgence of rhabdomyolysis (CPK 26100 U/L to 308612 U/L) and transaminitis (AST 426 U/L–1649 U/L) on day 5. Gastrocnemius muscle biopsy demonstrated rare atrophic fibers, without abnormal lipid accumulation, amyloid, enzymes deficiencies, necrosis, or inflammation. CPK and AST rapidly attenuated within 16 hours of discontinuing a propofol infusion, initiated 2 days prior when the resurgence first began. The patient made a full recovery after 96 days of hospitalization.

Conclusion: We report a rare case of multi-organ system failure following a single-dose MDMA ingestion. The metabolism of MDMA is mediated by CYP2D6. Propofol has inhibitory effects against CYP2D6 as well as against mitochondrial toxicity.[1,2] We observed an unexpected resurgence in rhabdomyolysis and transaminitis, associated with the initiation of propofol, and attenuated upon its discontinuation. Future identification of patient CYP2D6 phenotypes and forensic analysis of xenobiotics ingested will better define this association.

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185. Drug-facilitated sexual assaults in Italy: Preliminary data of the Violence And Date Rape Drug project

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Objective: The aims of the VARD project (Violence And Date Rape Drug) are to evaluate the cases of DFSA (Drug-Facilitated Sexual Assault) in Italy and to identify the profile of drugs of abuse involved in the cases of sexual assault.

Methods: In a prospective study (2011–2014), patients seeking health care after sexual assault and for which the Pavia Poison Control Centre (PCC) is called from the emergency departments or sexual assault centers all over Italy are included. The inclusion criteria are partial/complete amnesia for the alleged assault and/or (i) suspicion of covert drug administration and/or (ii) voluntary intake of alcohol or drugs and/or (iii) signs/symptoms of intoxication. In each case, the PCC evaluates the characteristics of the DFSA and the clinical picture, and collects the victims' biological samples which are subsequently analysed at the Institute of Legal Medicine, Catholic University, Rome. The study had the approval of the ethical committee of every participating center, and informed consent was obtained in all the recruited cases.

Results: Fifty-one patients were included from November 2011 to September 2013 and reported as preliminary results (mean age, 26 years; 99% females): 34 patients (66%) reported the suspicion of covert drug administration, and 24 patients (47%) admitted voluntary consumption of drugs of abuse. Seven patients (13%) presented signs of intoxication (sedation in 3 cases; vomiting, nausea, headache, mydriasis, tachycardia, and abdominal pain in one case each). Seventeen patients (33%) did not show any type of injury (genital or other). Samples were collected between 3 and 72 hours after the violence. Ethanol was found in blood in 17 cases (33%) and urinary ethyl-glucuronide in 28 (55%). Other

detected substances were benzodiazepines (11 cases), cocaine/benzoylecgonine (5 cases), tetrahydrocannabinol (3 cases), morphine, methadone, and venlafaxine (1 case each).
Conclusion: Ethanol, sedative drugs, or drugs of abuse are frequently detected in samples collected from victims of sexual assault. The absence of injury or signs and symptoms of intoxication at the time of the medical examination do not exclude a DFSA.
Acknowledgements: The study was carried out with the support of the Department of Antidrug Policy—Presidency of the Council of Ministers.

186. Misuse and abuse of fentanyl depot transdermal patches

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Objective: To illustrate the spectrum of unintended use of fentanyl patches and the dangers involved.
Methods: All fentanyl cases reported to the Swedish Poisons Information Centre (PC) during the years 2000–June 2013 were analyzed regarding age, gender, reason for the overdose, routes of exposure, and outcome.
Results: Among a total number of 202 inquiries to the PC concerning patients with symptoms related to fentanyl, patch formulations were involved in 183 (91%) of the cases. Males were slightly over represented. The majority of patients were adults, 23 were older than 70 years, 2 were children, and only one teenager. In 74 (41%) cases, it was apparent that drug addiction was the reason for the exposure. Already used fentanyl patches contain as much as 30–85% of the active substance and are therefore a potential source for opiate misuse. The route of exposure in this subgroup was oral, swallowed or chewed (39%), intravenous injection of patch content (24%), smoking of the patch (15%), dermal (12%), combined applications (mostly dermal + oral 8%), and rectal in one case. Accidental overdosing occurred in 53 (29%) cases and was the most common cause of poisoning in elderly people. Multiple patches were applied due to forgetfulness or, in some cases, chewed by patients suffering from dementia. Suicide attempt was the reason for the overdose in 38 (21%) patients. In 11 (6%) cases, the symptoms were related to application of the prescribed therapeutic doses whereas the aetiology remained unclear in a few instances. In hospital severe opiate symptoms, when present, were treated with naloxone and in a few cases respiratory support. Deaths were not reported.
Conclusion: Fentanyl depot patches, including those already used, can be misused in various ways and the risks involved are considerable. Although not observed here, fatalities have been reported elsewhere. Elderly people are at higher risk of accidental overdoses and it can be questioned whether this fentanyl formulation is suitable for this age category. Health care providers need better routines for the handling and discarding of already used fentanyl patches.

187. Severe intoxication after hidden chronic abuse of liquorice: A case report

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Objective: Liquorice, derived from the root of *Glycyrrhiza glabra*, is available in various forms. It is a popular sweetener added to different foods. To describe a clinical course of chronic hidden liquorice abuse, confirmed by quantitative determination of glycyrrhetic acid.
Case report: A 55-year-old woman presented to the emergency department for nausea, abdominal pain, and vomiting started 1week before. Medical history was negative for the consumption of drugs. At first clinical evaluation, the patient was apyretic and drowsy, blood pressure of 130/110 mmHg with normal heart rate, and oxygen saturation in room air. Arterial blood gases revealed: pH 7.2, HCO_3 12.1 mmol/L, PCO_2 31 mmHg, PO_2 94 mmHg, base excess -14.7 mmol/L, and K^+ 1.2 mmol/L. The clinical course was characterized by metabolic acidosis, mild rhabdomyolysis (440 U/L), pancreatitis (α-amilases, 763 U/L), and renal failure (creatinine, 2.4 mg/dL). Abdominal ultrasonography was normal. First diagnosis of acute pancreatitis associated with severe hypokalemia and renal tubulopathy was made. The neurological conditions rapidly worsened and coma associated with tremors and muscle paralysis appeared. The woman required oro-tracheal intubation and mechanical ventilation. A severe bilateral weakness of proximal and distal muscles of all 4 limbs (symmetric flaccid paralysis) was present. At this time, her brother mentioned consumption of herbal products for the last 20 years, comprising laxatives, diuretics, caffeine, metformin, and appetite suppressants (such as amphetamine-like drugs). Moreover, the patient had taken 2 tablespoons of liquorice powder once a day for the last few months. Specific treatment with potassium supplementation and continuous venovenous hemodiafiltration (CVVHDF) were started. Complete clinical resolution of neurological complications was registered in 18 days. The blood levels of glycyrrhetic acid were 63 and 65 ng/mL at 4th and 7th hospitalization days, respectively.
Conclusion: People consume liquorice because it is credited with possessing healthy properties, and the potential hazards of overconsumption are ignored. In particular, chronic consumption of liquorice can cause symptoms similar to those of mineralocorticoid excess and suppression of the renin-aldosterone system. Patients with hypertension, hypokalemia, and metabolic/neurological disturbances require differential diagnosis procedures including advanced laboratory support to exclude liquorice intoxication.

188. Blood lead levels in opium addicts in Mashhad, Iran

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Objective: Adulterated opium is one of the new sources of lead exposure in our region.[1] Recently reported findings suggest lead toxicity in opium addicts referred with unspecific symptoms.[2] As far as the literature review is concerned, there are limited studies

assessing the prevalence of toxic lead levels in this subgroup of the population. In our study, evaluation of blood and urine lead levels and probability of lead poisoning and also the relation between serum lead levels and the duration and pattern of addiction in a group of oral/inhaled opium addicts was investigated.

Methods: Ethics approval was obtained from the Ethics Committee of the Mashhad University of Medical Sciences (MUMS/91/88713). Considering inclusion and exclusion criteria, blood and urine lead levels of 40 subjects, comprising of patients who used oral and inhaled opium with a mean age of 43 ± 10.15 years, were evaluated. For lead level assay, 3 mL of whole blood and urine were obtained and lead level was assessed immediately using an atomic absorption spectrophotometer.

Results: The mean value of blood lead level in the study group was 7.14 ± 1.41 micrograms/dL, and the mean value of urine lead level was 2.62 ± 0.83 micrograms/dL. There was no significant correlation between blood lead level with duration of opium ingestion ($p = 0.26$) and pattern of addiction ($p = 0.25$). There was also no significant correlation between urine lead level with duration of opium ingestion ($p = 0.28$) and pattern of addiction ($p = 0.26$).

Conclusion: In this study, the mean value of blood lead level in opium addicts was higher than mean values obtained in population-based studies but lower than toxic level. The relation between serum lead level and duration and pattern of addiction was not significant. Similar investigations with larger sample size and comparative studies with healthy controls are suggested.

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189. Full of grace to full of gas: A perforated body packer

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Objective: Body packers ingest large numbers of drug-filled packets to smuggle drugs across international borders. Although mechanical bowel obstruction and perforation are described, every previously reported case of bowel perforation resulted in death. We describe the first case of survival in a body packer with developed intestinal perforation.

Case report: Law enforcement agents brought a 28-year-old man suspected body packer to the emergency room who complained of abdominal pain and vomiting for a day. He reportedly ingested 17 thumb-sized, heroin-filled packets four days earlier in Los Angeles. He denied use of agents to slow gastrointestinal motility and his last bowel movement 24 hours earlier, contained no packets. Vital signs were blood pressure, 150/80 mmHg; heart rate, 84 beats/min; respirations, 18/min; oxygen saturation, 98% on room air, and temperature, 36.6°C. Physical examination revealed no toxidrome, distant bowel sounds, and diffuse abdominal tenderness without guarding. Computed tomography (CT) scan with contrast demonstrated at least ten packets within the small bowel with partial obstruction, and small foci of mesenteric air with fat stranding, suggestive of micro-perforation. He underwent surgical retrieval of 17 firm, intact packets of heroin. A small bowel resection with primary anastomosis was performed. His post-operative course was uneventful, and he was subsequently discharged to custody.

Conclusion: We believe this to be the first reported non-lethal case of bowel perforation from heroin body packing. Although the majority of cases with adverse events following body packing are caused by intoxication from drug leakage, improvements in packing techniques may decrease this risk and increase the incidence of bowel obstruction and perforation. While abdominal pain and distension are likely common in body packers, we speculated that bowel perforation was identified and treated promptly in this case because of a high index of suspicion, findings on physical examination, and early imaging by CT. These factors may lead to early identification of bowel complications and reduce associated morbidity and mortality.

190. Consumption pattern of party drugs in Denmark

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Objective: Party drug consumption is a growing problem in Denmark. Often these drugs are taken in combination. We therefore set out to describe the consumption pattern of party drugs through experiences from the Danish Poison Information Centre (DPIC).

Methods: Between January 2006 and May 2013, DPIC received 112,000 telephone contacts. We searched the DPIC database for contacts which involved substances such as amphetamine, ecstasy, ketamine, cocaine, lysergic acid diethylamide (LSD), psilocybin, mescaline, and gamma-hydroxybutyrate (GHB).

Results: During the study period, DPIC had 3360 contacts which involved party drugs, representing a total of 3102 poisonings. Party drug consumption was clearly a weekend phenomenon—half of the contacts were on Saturdays and Sundays ($P < 0.0001$). Table 1 shows the most commonly used drugs and how these were combined: amphetamines or ecstasy were used in 56% of the party drug poisonings, and were often combined with cocaine, cannabis, or benzodiazepines. In 4% of the poisonings, patients were co-medicated with antipsychotics or antidepressants. However, combinations with other kinds of prescription drugs were negligible.

Conclusion: Combining different party drugs and psychopharmacological prescriptions is common. The majority of these combinations hold the potential for severe pharmacodynamic or pharmacokinetic interactions. However, the volume of scientific literature in the field is sparse. Despite the limitations associated with retrospective data from PICs, our data emphasize the importance of evaluating drug–drug interactions for risk assessment.

Table 1. The most commonly used drugs and combinations.

Column percentages	Amphetamine/ ecstasy	Cocaine	GHB	Hallucinogenics	Ketamine
Amphetamine/ ecstasy		29.7%	20.6%	23.1%	31.4%
Cocaine	15.9%		13.8%	11.9%	15.7%
GHB	6.8%	8.6%		4.0%	9.9%
Hallucinogenics	3.7%	3.6%	1.9%		4.5%
Ketamine	4.1%	3.8%	3.8%	3.6%	
THC	11.1%	10.5%	4.5%	15.2%	8.1%
Benzodiazepines	9.2%	10.0%	4.5%	4.3%	4.5%
Antidepressants	2.2%	2.6%	0.3%	1.4%	0.4%
Antipsychotics	3.2%	2.7%	1.2%	0.7%	0.4%
Opioids	5.7%	9.7%	1.6%	4.0%	2.7%
Total	1726	922	572	277	223

191. Withdrawal from massive diphenhydramine abuse

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Introduction: Massive abuse of diphenhydramine (DPH) has been very rarely described in the past. Some users claim that it gives them a clarity of thought unlike any other substance of abuse.
Objective: Describe a case report of withdrawal from massive DPH abuse.
Case report: A 61-year-old female, with history of opiate abuse (on Suboxone), compulsive soda drinking, remote ethanol abuse, and nicotine addiction, admitted to her daughter to be surreptitiously ingesting up to sixty 25-mg tablets of DPH daily for at least 6 months and possibly a couple of years, "just to help her sleep". Her daughter located discount store receipts documenting the purchase of 23 bottles containing 600 tablets of 25-mg DPH over the past 3 months. Upon discovery, her daughter insisted that she completely stop taking DPH. The patient became gradually more delirious, agitated and diaphoretic, and was brought to the emergency department (ED) by her daughter. In ED, vital signs such as heart rate, 95 bpm; blood pressure, 122/63 mm Hg, in "severe distress." Except for K of 3.2 mEq/L admission laboratories were unremarkable with negative tox screen except for positive buprenorphine and tricyclic immune assay. The ED physician called the poison center and asked whether to give physostigmine for possible anticholinergic poisoning from possible re-ingestion versus more DPH for possible withdrawal. The recommendation was to try supplemental DPH. Over the next 24 hr, the patient required 200 mg DPH intravenously (IV) every 4–6 h to reverse delirium. Her hospital course was notable for her refusing transfer to drug rehabilitation facility and regional detoxification and rehabilitation facilities declining to admit her for this addiction.
Conclusion: Massive DPH abuse has rarely been reported. Abrupt discontinuation of DPH may lead to withdrawal manifest as acute delirium, with agitation and diaphoresis. Carefully titrated doses of IV DPH were useful in controlling the delirium in this patient. Locating a drug rehabilitation facility comfortable with this type of addiction may also be problematic.

Table 1. Frequency of detection of CYP inhibitor medications and methadone in postmortem examinations.

Methadone plus	N = 42	%
Fluoxetine	11	3.6
Sertraline	11	3.6
Diltiazem*	10	3.2
Venlafaxine*	7	2.3
Paroxetine	5	1.6
Fluvoxamine	0	0

*One case had both diltiazem and venlafaxine detected

192. Analysis of overdose deaths involving methadone and cytochrome P450 inhibitors

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Introduction: Opioid-related deaths, including methadone, are currently the most common cause of unintentional drug overdose death in the United States. Co-ingestants are common, especially benzodiazepines. Few researchers have reported on co-ingestants that would interfere with the pharmacokinetics of methadone such as cytochrome P450 3A4 and 2B6 inhibitors.
Method: Retrospective analysis of consecutive deaths reported by a state Office of the Chief Medical Examiner (OCME) to a poison center. Inclusion criteria: deaths where methadone was detected in the postmortem examination, at any concentration. Exclusion criteria: persons under the age of 12 years.
Results: Over the 24-month study period, 1589 OCME deaths were reported to the poison center. Of these, 310 cases met the inclusion criteria; 2 met the exclusion criteria, leaving 308 cases for analysis. The median age was 42 years (range, 16–66 years), and 61% were male. The mean number of substances detected post-mortem was 3.74 (range, 1–9 substances). Of the 308 cases analyzed, 95.0% had at least one other substance detected besides methadone and 15 (4.8%) cases had methadone only. Methadone and one CYP inhibitor drug were detected in 42 (13.6%) cases. Methadone and two CYP inhibitor medications were detected in one case (methadone, venlafaxine, and diltiazem, Table 1).
Conclusion: In this retrospective analysis of consecutive postmortem examinations, the frequency of detection of other drugs besides methadone was 95%. The co-detection of methadone and at least one CYP inhibitor medication was 14%. Further research and efforts to curb opioid deaths should consider the problem of multidrug exposures and pharmacokinetic interactions.

193. A case of heroin overdose reversed by sublingually-administered buprenorphine/ naloxone film (Suboxone®)

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Objective: Buprenorphine is a partial mu opioid agonist with a high affinity for the receptor which enables it to displace most other opioids from the receptor. A case of heroin overdose reversed by sublingually administered buprenorphine/naloxone(Suboxone®) tablet has been previously described.[1]
Case report: An individual who is prescribed buprenorphine/naloxone film (Suboxone®) witnessed a friend overdose on heroin. The victim, a 22-year-old Caucasian male, reportedly had rapidly injected "$30 worth of heroin" and, within several minutes, "he was barely breathing, a few times a minute, and his lips turned blue." "He wouldn't wake up even when I rubbed his chest hard." Others present reported that the victim had not used any benzodiazepines, prescription opioids, other illicit substances, or alcohol that day. The individual who was prescribed buprenorphine/naloxone had one of his 8/2 mg sublingual films with him and, knowing that it can precipitate withdrawal, decided that it might reverse the overdose in this case. He placed the victim on his side, removed the film from the child-proof foil package, moistened it, placed it under the victim's tongue, and "moved his tongue around so it would dissolve quicker." "Within two to three minutes, he started breathing more normally and woke up." Although first responders were called, the victim refused transport to the hospital. The friend remained with the victim for several hours during which "he was fine; he never went back out."
Conclusion: Sublingually administered buprenorphine/naloxone film appears to be able to reverse an opioid overdose. The manufacturer reports that the film formulation dissolves more rapidly and reaches a higher maximum plasma concentration than the tablet, allowing for more rapid absorption and action of the buprenorphine (naloxone is minimally absorbed sublingually). Although not approved for this indication, it might be useful for programs concerned with public health issues related to opioid use (such as overdose prevention) to be aware of the potential use of buprenorphine and buprenorphine/naloxone for the reversal of opioid overdose in life-threatening situations where no other option is available.

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194. Estimation of heavy metals in different brands of moisturizers and lipsticks using atomic absorption spectroscopy

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Introduction: Cosmetics are care substances used to enhance the appearance or odor of the human body. They are generally mixtures of chemical compounds, derived from natural sources or many being synthetic products. Different cosmetics such as creams, lotions, shampoos, hair oils, hair dyes, perfumes, lipsticks, and eye liner are available for use without proper information on labels regarding its contents and composition. Human exposure to heavy metals from these cosmetic products can lead to acute and more often chronic toxicity. Heavy metals are a part of coloring agents, oxidizers, or stabilizers added to cosmetic products. Thus, it is important to monitor the heavy metal concentration in cosmetic products to ensure health safety on repeated use.
Objective: The objective of the study was to estimate the levels of heavy metals (lead, cadmium, nickel, and zinc) and metalloid (arsenic) present in cosmetic products using atomic absorption spectroscopy (AAS).
Methods: Two batches of ten brands of lipsticks and moisturizers were obtained from the local market. A total number of 40 samples were analyzed in duplicates for lead, cadmium, nickel, zinc, and arsenic. Flame atomizer and hydride generator were used for heavy metal and metalloid (arsenic) analysis, respectively, against the commercially available standards.
Results: The concentration of heavy metals in moisturizers was as follows: lead (0.0250–0.1348 ppm), zinc (0.0250–0.1348 ppm), nickel (0.0118–0.0484 ppm), and arsenic (0.0412–1.2271 ppb). In lipsticks, the concentration estimated was lead (0.0181–0.2386 ppm), zinc (0.0065–0.7311 ppm), nickel (0.0137–0.5548 ppm), and arsenic (0.3641–1.5367 ppb). The levels of all the heavy metals were more in lipsticks than in moisturizers but within the permissible limits. Cadmium was undetectable, both in moisturizers and in lipsticks.
Conclusion: Though the analysed concentrations of heavy metals are well within the permissible limits, they have the potential to cause some serious side effects on chronic use. The various brands contain different concentrations of heavy metals, which necessitates periodic testing to monitor the toxic heavy metal contaminants in cosmetic products, protecting human health.

195. A case of intravenous injection of mercuric chloride

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Objective: Mercuric chloride is one of the most toxic mercury salts. Mercuric salts are corrosive and nephrotoxic. Mercuric chloride poisonings have been reported in which intoxication followed ingestion, inhalation, or dermal contact, but intravenous (IV) administration of mercuric chloride is very rare.
Case report: A 24-year-old healthy female, amphetamine abuser, injected accidentally 300 mg of mercuric chloride instead of amphetamine. She also ingested a small amount. Three days after exposure, the patient was admitted to hospital and had nausea, vomiting, abdominal pain, visual disturbances, joint pain, and anuria. After arrival, her plasma creatinine level was very high, 900 micromol/L (normal, 50–90 micromol/L). Furosemide and intravenous fluids were immediately given but failed to initiate diuresis, so hemodialysis was started. Two days after admission to the hospital, her blood mercury level was extremely high, 11,246 nmol/L (normal $<$ 10 nmol/L). Analysis of subsequent samples failed due to problems in the laboratory. The patient stayed 4 days in the intensive care unit (ICU). Chelation therapy (DMSA) was given for 32 days. For the first two days, the antidote was given intravenously in the ICU and after that orally, continuing even at

home. Diuresis recovered after several days and the dialysis could be discontinued. Plasma creatinine levels decreased slowly. Twenty-seven days after exposure, the patient's plasma creatinine level was 128 micromol/L, almost in the normal range, and she was discharged. Kidney biopsy was planned for later, but the patient was noncompliant and did not come to hospital or answer any calls.
Conclusion: Injection of mercuric chloride can cause a severe poisoning with acute renal failure, but with antidote treatment and good supportive care, the patient can recover.

196. Skin-whitening cream-related mercury poisoning treated with dimercaptopropane sulfonic acid

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Background: Exposure to topical mercury-containing compounds can result in systemic absorption and toxicity. We report a case of mercury poisoning following topical use of a herbal freckle-removing facial cream. Toxicological investigation confirmed the diagnosis and showed the effect of 2,3-dimercaptopropane-1-sulfonate and N-acetylcysteine.
Case report: A 50-year-old woman had been using a herbal freckle-removing facial cream for two months, and presented with symptoms of facial numbness and tingling pain, worsening tension headaches, fatigue, nervousness, and severe dry itchy eyes. The facial cream was found to contain 2.7% mercury by weight. The patient's initial blood and spot urine mercury concentrations were 33.5 μg/L and 39.6 μg/g creatinine. She was advised to stop using the facial cream and prescribed oral N-acetylcysteine. Her blood mercury concentration decreased to 15.5 μg/L and spot urine mercury concentration rose to 87.4 μg/g creatinine 2 weeks later. Intravenous N-acetylcysteine and 2,3-dimercaptopropane-1-sulfonate acid treatment were initiated, the pre and post-chelating urine mercury concentrations were 72 and 2,262 μg/day, respectively. Her symptoms resolved following chelation.
Conclusion: This patient with moderate mercury poisoning appeared to have benefited from 2,3-dimercaptopropane-1-sulfonate acid and N-acetylcysteine treatments, with 30-fold increase in urinary mercury excretion and clinical recovery.

197. Subcutaneous elemental mercury injection and bone marrow failure: A fatal case

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Objective: Elemental mercury (Hg) injection is rarely reported in the literature, especially self-inflicted administration. Toxicity is primarily local with intense inflammation that may occur several months after the event. Systemic toxicity involves renal or neurological impairment and life-threatening conditions such as pulmonary embolism.[1] Here, we describe an unusual fatal bone marrow failure after elemental mercury injection.
Case report: A 46-year-old woman presented to the emergency department complaining of weakness and slight fever. Blood tests showed severe anemia (Hb 2.9 g/dL), thrombocytopenia (platelet blood test [PLT], 2000/mm^3), and leukopenia (white blood cells [WBC], 3180/mm^3). A further inquiry revealed that the patient 8 months before had self-injected subcutaneously metallic mercury into her left-forearm resulting in a massive abscess, drained 4 months later. Four months after the surgical intervention, an X-ray showed the persistence of metallic mercury at the injection site. Blood and urinary mercury levels were 85 micrograms/L (normal,$<$4.5) and 914 micrograms/L (normal,$<$5), respectively. The metal speciation revealed the presence of elemental mercury. Samples of bone marrow detected a marked reduction of cell presence. After the treatment with meso-2,3-dimercaptosuccinic acid (DMSA), plasma Hg level decreased significantly and a transient increase in liver function markers was reported. The patient presented a posterior reversible encephalitic syndrome that lasted a few days. Treatment with immune suppressants and thrombopoietin receptor agonist was performed unsuccessfully. Six months later, the patient developed a severe fatal pulmonary infection.
Conclusion: Pancytopenia has been rarely reported after elemental mercury injection. Indeed, in the last 10 years, only one case of bone marrow failure was described following intravenous mercury administration.[2] Nevertheless, in the circulatory system, elemental mercury can be transported to every organ with subsequent multi-organ toxicity. In our case, a possible association between mercury toxicity and fatal bone marrow suppression could be suggested.

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198. Elevated blood lead levels among adolescents pursuing the sport of firearms marksmanship

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Objective: Marksmanship has grown in popularity among American youth. We present two cases of lead poisoning associated with this sport.
Case series: Case #1: A 16-year-old male presented with an elevated blood lead level (BLL) 32 micrograms/dL (1.5456

micromol/L [repeated twice: 27 (1.3041) and 24 (1.1592) micrograms/dL (micromol/L)]. He denied symptoms of lead poisoning; there were no other sources of exposure. He had attention deficit hyperactivity disorder (ADHD) well controlled on medicine; physical examination was unremarkable. BLL was 23 micrograms/dL (1.1109 micromol/L); zinc-chelated protoporphyrin (ZPP) levels, blood count, and iron studies were normal. He was a competitive precision shooter specializing in 22-caliber rifles, competing regionally and nationally for 2 years. He attended indoor ranges 3x weekly, 3–4 hours/session, during fall and winter months. Ventilation and air filtering at one range seemed "substandard." He cleaned the floor of bullet casings by dry sweeping between sessions. He wore protective equipment and shot in several positions: standing, kneeling, and prone. When prone, he lay on a mat, which was not routinely cleaned. After preventive counseling, his BLL dropped to 17 micrograms/dL (0.8211 micromol/L). Case #2:A 16-year old male was referred for BLL 20 micrograms/dL (0.966 micromol/L). Patient disclosed that he was an expert marksman shooting on a range of 3–4 times weekly as a member of a junior rifle team. He shot in the standing and prone positions with shotguns. The family enjoyed recreational shooting and was active in the local gun club. The indoor range used a high-efficiency particulate absorption (HEPA) ventilation system, but staff only dry swept interior surfaces. He was asymptomatic; physical examination was unremarkable. Pediatric Environmental Health Specialty Unit (PEHSU) recommended good hygiene, protective clothing, and avoidance of ranges with poor cleaning and inadequate ventilation. Follow-up BLL declined to 17 (0.8211), then 15 (0.7245) micrograms/dL (micromol/L) over 4 months. Patient no longer practiced on mats or while recumbent; the rifle club had closed.

Conclusion: While the hazard of lead exposure is well known among the military and police participating in regular target practice, the risk is under-appreciated among pediatric recreational or competitive marksmen. We recommend routine BLL screening for youth marksmen. Hygienic and preventive measures can lower their risk of lead poisoning.

199. Blood lead levels and haemoglobin concentration in children below 5 years in Ajman, United Arab Emirates

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Objectives: Environmental exposure to lead is commonly encountered in children leading to acute and chronic toxicity. Measuring lead levels in the blood is considered as a good indicator of lead burden in the body. The objectives of the study were to estimate the blood lead levels and correlate them with the hemoglobin, age, and body weight and identify the potential sources of lead exposure in children.

Methods: Following ethical approval, blood samples were collected from 53 children aged between 1 and 5 years and analyzed for hemoglobin, and lead levels (BLL) using graphite furnace atomic absorption spectrophotometer. An eight-item questionnaire was used to identify potential sources of lead exposure.

Results: The mean BLL and haemoglobin concentration in children was 6.4 micrograms/dL and 11.9 g/dL. Children with 5–10 micrograms/dL BLL had higher prevalence of anemia (29%). However, there was no correlation between BLL and hemoglobin. The BLL were higher in children between 1 and 3 years but did not show a significant difference as compared to other age groups. The commonest cause of lead exposure identified was sucking of cheap toys rich in lead content followed by contact with kohl.

Conclusion: The blood lead levels were higher when compared with international safety guidelines. Since lead has a zero threshold for toxicity, children below 5 years of age should be screened for blood lead levels to avoid adverse effects on physical development, behavior, intelligence, and learning abilities. In addition, necessary steps should be taken to identify and terminate the exposure to lead sources protecting them from acute and chronic toxicity.

200. Cases of self-poisoning with elemental mercury administrated intravenously: Clinical observations

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Objective: Poisoning by injection of metallic mercury is uncommon and considered relatively harmless versus ingestion of mercury salts or inhalation of mercury vapor. This report presents two cases of intravenous administration of elemental mercury.

Case series: Case 1 – a man aged 31 years was admitted to Moscow Toxicology Center in January 2013 following intravenous administration of 4 mL of elemental mercury 4 days previously. Earlier in 2010, he had administered mercury intravenously and was treated in another hospital for 20 days. On admission, he complained of weakness, nausea, respiratory, and sleep disturbance. Chest X-ray demonstrated numerous small focus-like shadows of metallic density. Inductively coupled plasma spectrometry detected a blood mercury level of 193 microgram/L (norm, 0.2–5.8 microgram/L). Chelation therapy with 2,3-dimercapto-1-propanesulfonic acid (DMPS) was started and one procedure of hemodiafiltration was performed. Renal function was not disturbed. There were no symptoms of toxic encephalopathy or polyneuropathy. The final results of therapy were unknown as the patient self-discharged. Case 2 – a man aged 22 years was admitted to Tbilisi Toxicology Center, Georgia, in November 2012, 4 months after premeditated intravenous injection of elemental mercury from several medical thermometers. After an asymptomatic period of 2 months, the patient began to complain of pain and tremor in limbs, fatigue, and skin rash. Computed tomography (CT) scan of the thorax and the abdomen detected multiple small opacities of metallic density in the both the lungs, liver, right kidney, and wall of the heart. Therapy with DMPS was started at a dosage of 20 mg/kg/day and then continued after the patient had been transferred to the toxicology center in Baku, Azerbaijan. On admission, no biochemical abnormalities in hepatic or renal function or clinical pulmonary malfunction

were detected despite the presence of erethism, mercury tremor, pain in knee joints, and muscle weakness of lower extremities. After 1 month of chelation therapy, mercury blood concentration decreased from initially 134 micrograms/L to 105 micrograms/L (normal, 4.00–5.00 micrograms/L by X-ray fluorescence analysis (XFA) spectrometry).
Conclusion: These case reports demonstrate mild acute toxicity following intravenous administration of elemental mercury. Clinical manifestations of mercury intoxication administered intravenously may be delayed despite significantly increased mercury blood levels.

201. Arsenic elimination in the urine after crustacean ingestion

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Objective: Urinary elimination of arsenic (mainly non-toxic arsenobetaine) following seafood ingestion has been poorly described. Thus, it remains difficult to determine the optimal time frame in which to evaluate a patient for possible arsenic toxicity when seafood has recently been consumed. The United States Agency for Toxic Substances and Disease Registry (ATSDR) in addition to most major laboratories recommend abstinence from all seafood for 48 hours prior to urinary arsenic analysis. The objective of this study is to determine when urinary arsenic returns to normal reference concentrations following crustacean ingestion and to describe its elimination kinetics.
Methods: Seven healthy adult subjects abstained from seafood ingestion for a week prior to the study and throughout the study collection period. Following baseline urine sample collection, subjects ate a meal of American Gulf Coast shrimp. The total weight of shrimp consumed was calculated for each subject. Subjects collected urine samples every 8 hours for days 1–3 and then daily on days 4–6. Urine arsenic concentrations were determined by inductively coupled plasma-mass spectrometry and normalized to urine creatinine concentrations (determined by an enzymatic colorimetric assay). An abnormal arsenic to creatinine concentration was defined per the manufacturer's reference as greater than 35 micrograms/g.
Results: Six of seven (86%) subjects had undetectable arsenic concentrations at baseline (one subject had a baseline concentration of 175 micrograms/g despite abstaining from seafood). The initial 2 hour post ingestion arsenic concentrations ranged from 60 micrograms/g to 784 micrograms/g (mean, 356 micrograms/g). The total weight of shrimp consumed did not predict post-ingestion arsenic concentrations. At 48 hours post ingestion, 4 of 7 (57%) of the subjects had elevated abnormal concentrations. At 64 hours, 2 of 7 (29%) had abnormal elevated concentrations; all participants had concentrations within the reference range at 80 hours post-ingestion. The mean elimination half-life was 17.6 hours with a standard deviation of 3.7 hours.
Conclusion: In this pilot study, abnormal urine arsenic concentration following crustacean ingestion persisted in healthy volunteers for up to 80 hours. Health care providers should consider having patients abstain from seafood longer than the 48-hour recommendation given by most laboratories and the Agency for Toxic Substances and Disease Registry (ATSDR) before testing for urinary arsenic.

202. Elemental mercury exposures: A review of enquiries to the New Zealand Poisons Centre

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Objective: Public concern regarding mercury toxicity has heightened over recent years, with attribution of a variety of symptoms to mercury poisoning, even from low exposure scenarios. This study was undertaken to characterize the type of exposures to metallic mercury that prompted enquiries to the New Zealand National Poisons Centre (NZNPC), and to assess the risks from such exposures.
Methods: A retrospective analysis was undertaken of all enquiries to the NZNPC regarding mercury, for the 6-year period between January 2007 and December 2012. Relevant data were retrieved from the Calls Database, and categorized according to various demographic and exposure variables.
Results: A total of 1234 enquiries occurred over the 6-year period, equating on average to nearly four calls per week. The great majority were from members of the public (85.4%), with 14.6% from health professionals. Some incidents prompted more than one enquiry. With 1188 enquiries (96.3%), there was either direct exposure or a spill with at least the potential for exposure, while 46 (3.7%) were requests for information only. Overall, 56.6% involved mercury thermometers, 24.7% compact fluorescent light bulbs, 3.5% sphygmomanometers, 0.7% mercury switches, and 14.5% other sources of mercury. With the thermometer exposure calls, 94.6% related to exposures in the home, with only 2.8% in a workplace setting (typically medical care facilities), and 1.3% in schools. For these enquiries, exposure mainly occurred via ingestion (63.1%), inhalation (17%), or skin contact (17%). Symptomatology at the time of the call was generally unremarkable.
Conclusion: The single most frequent enquiry concerned the accidental ingestion of mercury by an infant or child, from breakage in the mouth of a thermometer, in the home. While this scenario *per se* is generally of low hazard, the potential exists for inadequate or inappropriate clean-up, with risks of chronic mercury exposure and toxicity. This can be obviated by Poisons Centre advice on suitable clean-up protocols, but individuals may not always enquire at the time of the incident. The most appropriate solution would involve increased uptake of alternatives to mercury in medical devices.

203. Mercury bichloride iatrogenic poisoning

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Objective: We present a rare case of acute poisoning from mercury bichloride which was used for peritoneal washing during gynecological surgery to remove an ovarian teratoma.

Table 1. Treatment of mercury poisoning with chelating agents.

Day from poisoning	Treatment	Serum Hg level (micrograms/L)	Urine Hg level (micrograms/L)
4th	BAL: 3 mg/kg/4h IM × 2 days + hemodialysis	950	550
6th	BAL: 3 mg/kg/6h IM × 2 days + hemodialysis		
11th	BAL: 3 mg/kg/12h IM × 6 days + hemodialysis	650	70
14th	Succimer: 10 mg/kg/8h per os × 5 days + hemodialysis	450	50
19th	Succimer: 10 mg/kg/12h per os × 14 days		
26th	>>	262	60
35th	3 days after discontinuation of succimer	135	40

Case report: A call to the Poison Control Centre (PCC) for a 30-year-old woman with ileus, renal failure, and hemodynamic instability. Two days before, she had undergone surgery to remove an ovarian teratoma. Due to tumor rupture and suspected malignancy, the gynecologist conducted abdomen washing with a solution of mercury bichloride. Because of the severe condition, a second surgery was carried out the next day for possible surgical complications. Necroses were found in the omentum and intestine. It was reported to the PCC that mercury bichloride had been used in the first surgery. Instructions were given to measure levels and for the initiation of treatment with chemical agents (initially BAL and subsequently succimer) with instructions for reevaluation of levels in 14 days and to continue treatment if necessary. The patient had treatment for about 1 month as is shown in Table 1, and then she was discharged in good clinical condition with creatinine = 1. Instructions had been given for reevaluation in 14 days and continuation of treatment, but neither was done. One month later, the patient had incidents of tonic-clonic spasms. After our recommendation, she began treatment again with succimer (serum level, 26.5 micrograms/L; urine, 35.5 micrograms/L). Two months later, the latter level was 7.6 micrograms/L. She did not have repeated spasms.
Conclusion: Old treatment methods that have been removed and labeled as dangerous in the literature since the 1970s and 1980s may rarely cause serious poisonings. We must be able to recognize them.

204. Can bolete poisoning promote gastrointestinal bleeding?

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Objective: Two years of mushroom poisoning surveillance led to the suspicion that more frequent gastrointestinal bleeding (GB) occurred after bolete consumption. The aim of this study was to test this hypothesis.
Methods: Case/non-case retrospective study based on records in the French poisoning information system (Sicap) between January 01, 2010 and December 31, 2011. Patients with a gastrointestinal syndrome after mushroom exposure were selected (vomiting or diarrhea ± dehydration signs or electrolyte, renal or hemodynamic imbalance). Patients with signs of another mushroom poisoning syndrome were excluded (i.e., cyclopeptide syndrome). A case was defined after review of the data file by the presence of GB selected from 1) coding of the following Sicap thesaurus symptoms: hematemesis, intestinal bleeding, melena, or 2) presence in the free-text comments of any of the following terms (or their spelling variations): bleeding, blood, bloody, trace, hematemesis, and melena. Exposure to bolete was defined in the same way: 1) coding of the following agents: one of the 20 *Boletaceae* species listed, bolete, cep, unidentified mushroom with tubes, or 2) presence of the following terms: *Boletus*, bolete, cep, tube, pore. *Polyporus* species were excluded. After causality assessment, unlikely cases were excluded. Odds ratio (OR) of bolete exposure between cases (with GB) and non-cases (without GB) was computed.
Results: During this 2-year study, 2,096 patients presented a gastrointestinal syndrome. A GB was identified in 32 cases: hematemesis (n = 4), rectal bleeding (n = 4), or the combination of two (n = 2), single traces of blood in vomiting (n = 11), stool (n = 8), or the combination of two (n = 3). A bolete was identified in 961 of the 2,064 non-cases (47%) and in 30 of 32 cases with GB (94%, $p < 0.001$, OR 17.2; 95% CI, 6.0–49.3). Among these 30 cases, 3 cases were caused by raw bolete consumption and 12 cases were caused by exposure to *B.satanas* or a closely related species.
Conclusion: In the presence of a gastrointestinal syndrome, the risk of gastrointestinal bleeding is 17 times higher after eating bolete than eating other species. The importance of vomiting, the duration of diarrhea (mucosa irritation) and especially the ingestion of a red-pored bolete of the *B.satanas* group largely explain this risk.

205. Flagellate dermatitis due to raw shiitake consumption: A French Poison Control Centre study

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Objective: Shiitake mushroom (*Lentinus edodes*) is an edible fungus which was initially grown in Japan and China, and appeared more recently on the European market. A flagellate erythema may follow shiitake consumption and was first described in Japan in 1977.[1] The aim of this paper is to report a French case series.
Case series: A retrospective study of shiitake dermatitis cases, reported to the French Poison Control Centres (PCC) from January 2000 to November 2013, is presented. Among 32 exposed cases, 15 presented flagellate urticarial lesions after raw shiitake consumption. The first case of this series occurred in 2006, and the last 8 cases have been reported since 2012. During shared meals, no symptoms were observed among guests who pre-

ferred cooked shiitake to the raw mushroom. In this series, the rash appeared 12 hours to 5 days (median, 24 hours) after raw shiitake ingestion. Linear and itchy urticarial lesions appeared scattered on the trunk, arms, and legs within a few hours and persisted for 3–21 days. In 4 cases, rash and pruritus were either triggered or worsened by sun exposure. Eleven patients received corticosteroids, antihistaminic drugs, or both. All cases made a complete recovery.

Conclusion: Due to the rapidly increasing consumption of exotic food in Western countries, it is no surprise that cases of shiitake dermatitis are now appearing in Europe. The mechanism of shiitake dermatitis is thought to be toxic and due to lentinan, a polysaccharide component of the mushroom.[3] There is no specific validated treatment for shiitake dermatitis. Health professionals and the general population should be aware of both the risk associated with raw shiitake consumption and the good prognosis of this very spectacular and uncomfortable toxic dermatitis.

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206. Anticholinergic poisoning after drinking contaminated herbal tea

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Objective: To raise awareness of the risk of products of herbal origin. We report poisonings from drinking herbal tea containing marshmallow root (*Althaea officinalis*), which was inadvertently contaminated with an atropine-containing herb.

Case series: In January 2013, the Dutch National Poisons Information Center (DPIC) received an inquiry about a couple that fell ill within hours after drinking herbal tea, prepared with 20 grams of dried marshmallow root. Both developed dry mucous membranes, nausea, blurred vision, hallucinations, tachycardia, and urinary retention. They were hospitalized with evident anticholinergic symptoms that resolved after 4 days. The DPIC contacted the Netherlands Food and Consumer Product Safety Authority (NVWA), where one complaint was received about health effects after drinking a similar herbal tea. Within a week, 6 patients were reported to the DPIC and the NVWA, 4 were hospitalized and all recovered after 1–5 days without sequelae. The information gathered by the DPIC and the NVWA revealed that all involved products came from one supplier and contained *Althaea officinalis*. The NVWA contacted the supplier and indicated that the products should be withdrawn from the market, which was done within 3 days from the first case report. The supplier issued a warning to the public via advertisements in several newspapers. The DPIC posted a message via the EAPCCT to warn other Poisons Centers and to find out whether other European countries were having similar problems. Via the EAPCCT network, one case in France was identified, with herbal tea purchased in the Netherlands. Analysis of the products revealed a high atropine content (1–10 mg/g). Investigation of the production chain showed that contamination probably occurred during the harvest of *Althaea officinalis* in Bulgaria and the atropine source was deadly nightshade (*Atropa belladonna*). The contaminated batch was solely used in the Netherlands. The described incident occurred with a product from a renowned producer that practices quality control in the whole production process.

Conclusion: Contamination of herbal tea with *Atropa belladonna* can lead to serious atropine toxicity. Good cooperation between poison centers and health care authorities is essential to facilitate swift intervention measures and to prevent further harm to public health.

207. Major causes and prospects for prevention of poisoning or adverse events related to herbal medicines: Experience of a poison treatment centre in Hong Kong

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Objective: Herbal medicines, including traditional Chinese medicine (TCM) and proprietary Chinese medicine (PCM), are widely accepted and commonly used in Hong Kong. Investigation of herbal poisoning or herb-related adverse events is important for monitoring the safety of herbal medicines and evaluating prospect for prevention.

Methods: We report our experience of evaluating suspected TCM and PCM poisoning or herb-related adverse events at the Prince of Wales Hospital Poison Treatment Centre (PWHPTC), a tertiary referral centre for poisoning management in Hong Kong. All cases were evaluated by a team of clinical toxicologists with support from Chinese medicine pharmacists. Assistance was sought from the Hospital Authority Toxicology Reference Laboratory to perform analytical tests on the TCM/PCM or biological samples if indicated.

Results: From January 2011 to October 2013, 292 cases (male = 134, female = 158, age range: 7 days–106 years) were referred to PWHPTC for the assessment of suspected herbal poisoning or herb-related adverse reactions. After evaluation by clinical toxicologists with support from Chinese medicine pharmacists, 4 cases were considered likely to have and 11 cases with possible herbal poisoning or herb-related adverse events while the clinical conditions of 193 cases were considered unlikely to be related to herbal use or inconclusive. The other 84 cases had laboratory screening performed for further evaluation. Twenty-three of them were confirmed to have herbal poisoning or herb-related adverse events, and eighteen cases were confirmed to have problems related to PCM adulterated by Western drugs. Herbs containing aconitine alkaloids were the most common group of herbs involved in these cases. Common causes of herb-induced problems include misuse (inappropriate dosage or preparation), adulteration, contamination, and erroneous substitution.

Conclusion: A systematic approach to evaluate patients suspected to have herb-related poisoning or adverse events is important to establish the diagnosis and to evaluate the root causes. It also helps to monitor the safety of herbal medicines and implement effective strategies to safeguard the public.

208. *Peganum harmala* L. poisoning and pregnancy: Two case reports in Morocco

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Objective: *Peganum harmala* L., or "harmel,"is the most common plant used in traditional medicine.[1,2] The use of this plant during pregnancy can be particularly severe. We report two cases of *Peganum harmala* L. poisoning occurred in two pregnant women with good outcome.
Case series: Case 1: A woman aged 24 years, pregnant at 38 weeks of gestation without a medical history, was admitted to obstetric emergency for vomiting, abdominal pain, agitation, and consciousness disorders. History revealed the concept of taking harmel seeds to activate and facilitate delivery. Medical examination showed a confused patient, tachycardia at 120 beats/minute, without edema of the lower limbs; diuresis and proteinuria were normal. The obstetric examination revealed uterine hypertonia. Obstetric ultrasound was normal. Laboratory tests identified kidney failure. Delivery was very fast (one hour) giving birth to a newborn male with mild fetal and greenish amniotic fluid. Outcome was favorable for the child and the mother who confirmed the ingestion of harmel. Patient was discharged after a week of hospitalization. Case 2: An 18-year-old unmarried woman with amenorrhea was admitted to emergency department in an agitated state, with visual hallucinations, headache, and vomiting. Clinical examination revealed confusion (GCS 14), tachycardia 99 beats/min. Gynecological examination revealed a mean abundant reddish bleeding coming from the endocervix. Pelvic ultrasound showed an intrauterine pregnancy of 8 weeks of gestation and a trophoblastic detachment. Laboratory tests were normal. The patient was treated with diazepam, an antispasmodic and saline solution to 9%. The evolution was marked by improvement in neurological status at the 8th time and the bleeding stopped at the 24th hour. The patient revealed that she had ingested a tablespoon of *Peganum harmala* beans to induce an abortion.
Conclusion: *Peganum harmala* L. poisoning in pregnant women is a reality in Morocco. Obstetricians should be aware of this type of poisoning, and consider this diagnosis when faced with any uterine hypertension or unexplained placental abruption.

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209. Datura contamination of a large batch of frozen vegetables—some poisonings and a big hassle

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Objective: To describe an outbreak related to *Datura stramonium* contaminated frozen vegetables (expiration date July-October 2014) sold in the largest market chain in Finland May 2013.
Methods: Retrospective review of Finnish Poison Information Centre´s (FPIC) call records and 2 discharge reports.
Results: During May 2013, FPIC received 71 inquiries regarding mixed vegetables, contaminated by Datura seeds. FPIC received calls from concerned consumers (n = 57), media (n = 11), Finnish Food Agency (FFA), and the market chain (n = 3). We received 2 discharge reports related to calls and 2 separate case reports from hospitals after a warning notice was sent. The total number of suspected or confirmed poisonings was 28. Ten patients had symptoms. Before the contamination was detected, 2 patients were hospitalized: a 71-year-old woman and a 53-year-old man because of anticholinergic symptoms. An acute central nervous system (CNS) event was suspected, and they both underwent a computed tomography (CT) scan and the woman underwent also thrombolysis. After discharge, the woman noticed from a newspaper that the product she had eaten was recalled, because of the Datura contamination. The patient called back to hospital and FPIC was consulted. The man noticed while eating vegetables a strange pod mixed with the vegetables, but still ate it. FPIC distributed an electronic warning notice, about this possible cause of anticholinergic symptoms and the use of physostigmine for verification, to hospitals and physicians. The mixed vegetable batches were recalled, and the market chain used a database of its customer card owners and till-system to find customers who had bought the product. The database search was made with FFA authority permission. The market chain sent a warning notice to 30,000 customers to avoid using the product and to dispose of it. The outbreak was widely noticed by the media.
Conclusion: It can be difficult to differentiate anticholinergic symptoms without a plausible cause from cerebral blood circulation events (CBC). Treatment of CBC-events can have a higher risk than symptoms caused by *Datura* species. Without the recall, the outbreak could have been wider and lasted longer, because the frozen vegetables had a late expiration date. We are not aware of any new cases after May 2013.

210. Exposure to *Euphorbia lathyris*. Efficacy of an amphoteric washing solution

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Objective: We report the case of a patient with ocular and cutaneous burns with extreme pain following accidental exposure to *Euphorbia lathyris* latex. *Euphorbia lathyris* is a common biannual plant. It is also known by other names such as Mole Plant, Myrtle

Spurge and Gopher Spurge. It is prevalent in Europe, China, North America, and Australia.
Case report: A 58-year-old man attended the emergency department of Montbeliard Hospital in France with cutaneous and eye burns and severe pain. Patient's past medical history indicated fibromyalgia treated with morphine. He had already taken a tablet of oxycodone 10 mg, without any pain relief. After the first medical examination, he presented blepharospasm, face oedema, watering, and severe bilateral eye pain with EVA = 8 (Evaluation by the patient of the pain intensity: 0 = no pain, 10 = very severe pain). The offending plant was brought into hospital and was identified as *Euphorbia lathyris*. After traditional irrigation with saline solution, the patient still suffered terrible pain (EVA = 10). The patient's eyes were then rinsed with the amphoteric solution (250 mL in each eye). After 15 minutes, the blepharospasm disappeared (EVA = 6), and after 55 minutes, no more eye redness and no pain. An ophthalmology consultation showed only conjunctivitis.
Conclusion: Exposure to *Euphorbia lathyris* latex is a rare case of keratoconjunctivitis, corneal ulceration, anterior uveitis, and rarely blindness. In our case, only the amphoteric washing solution used calmed this patient exposed to the *Euphorbia lathyris* latex.

211. Do *Amanita muscaria* and *Amanita pantherina* poisoning differ?

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Objective: Ibotenic acid and muscimol are the main toxins in *Amanita muscaria* and *Amanita pantherina*. Ibotenic acid acts as an excitatory amino acid at glutamate receptors in the central nervous system (CNS), while muscimol is a GABA receptor agonist and therefore has a depressant effect on the CNS. After ingestion, ibotenic acid is metabolized to muscimol by decarboxylation. *Amanita muscaria* contains more ibotenic acid and less muscimol compared to *Amanita pantherina*. The aim of the study was to compare the clinical presentations in *Amanita muscaria* and *Amanita pantherina* poisoning.
Methods: In this retrospective study, we analyzed the clinical presentation of patients poisoned with *Amanita pantherina* and *Amanita muscaria* who were treated in the poison control centre (PCC) of Ljubljana University Medical Center in the past 30 years. The Mann–Whitney test was used for categorical variables. A p-value of less than 0.05 was considered as significant.
Results: Thirty-two patients poisoned with *Amanita muscaria* and 17 patients poisoned with *Amanita pantherina* were hospitalized in PCC Ljubljana during the past 30 years. Seventy-eight per cent (25/32) of patients poisoned with *Amanita muscaria* picked and ate a mushroom presumed to be *Amanita caesarea* and 41% (7/17) of patients poisoned with *Amanita pantherina* picked a mushroom presumed to be *Amanita rubescens*. The first symptoms presented themselves after the first 30 minutes–2 hours. Patients poisoned with *Amanita muscaria* were significantly more often confused (26/32, $p = 0.01$) and agitated (20/32, $p = 0.03$) compared to those poisoned with *Amanita pantherina* (8/17 and 5/17, respectively). On the other hand, patients poisoned with *Amanita pantherina* were significantly more commonly comatose (5/17) compared to those poisoned with *Amanita muscaria* (2/32, $p = 0.03$). There was no difference in hallucinations (10/32), myoclonus (6/32), convulsions (4/32), and vomiting (18/32) in patients poisoned with *Amanita muscaria* compared to those poisoned with *Amanita pantherina* (7/17, 6/17, 2/17, and 11/17, respectively) ($p > 0.05$).
Conclusion: *Amanita muscaria* containing more excitatory ibotenic acid results more often in confusion and agitation, while *Amanita pantherina* containing more inhibitory muscimol causes coma more often. Accordingly, the so-called ibotenic syndrome after *Amanita muscaria* and *Amanita pantherina* poisoning could be divided into two subtypes.

212. Surveillance of mushroom-related poisonings in Italy

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Objective: The National Poison Control Centre of Milan (NPCCM) handles each year about 1,000 inquiries concerning suspected mushroom poisonings. The present contribution is aimed at providing a preliminary characterization of these cases.
Methods: The NPCCM database was searched to identify all cases of mushroom exposure which occurred in 2000–2012. Each case was reviewed to assess the association between exposure and clinical effects. Mushroom names were standardized according to the scientific name of the species.
Results: In the period under study NPCCM handled 10,359 human cases of suspected poisoning due to mushroom ingestion. Most of cases (8,513, 82.2%) developed at least one sign/symptom possibly related to the reported exposure (cases of poisonings). Among these cases, 56% were aged 20 years or more, while subjects aged < 6 years or 6–19 years accounted for 4% and 7% of cases, respectively. Age information was missing for about 35% of poisonings since collective exposures were involved. Mushroom species were identified for 24% of poisonings, including *Boletus edulis* (503); *Amanita phalloides* (413); *Armillaria mellea* (403); *Inocybe/Clitocybe* (205); *Omphalotus olearius* (139); *Entoloma lividum* (97); and others (214). Some 66% of patients ingested unidentified mushrooms. However, those presenting with delayed gastrointestinal symptoms (i.e., 6 or more hours following ingestion, 20%) were assumed to be exposed to mushroom cytotoxins, e.g., amatoxins and orellanin. All together, 28% of patients suffered mushroom-related delayed effects, while 62% developed gastrointestinal signs/symptoms within 6 hours following mushroom ingestion. In all cases, the indication for treatment provided by NPCCT included gastric lavage, repeated doses of activated charcoal, and forced diuresis. The vast majority of cases showing delayed gastrointestinal effects (97%) were fully recovered within a week from exposure, while 3% developed severe effects including chronic kidney failure (26), liver failure requiring liver transplantation (13), and 27 died. All patients with rapid onset of clinical effects were fully recovered within 2–3 days.

Conclusion: Poison control centers are a relevant source of data for surveillance of mushroom-related poisonings. The available information can be compared at European level in order to define evidence-based treatments and support information and prevention programs.

213. Toxic risk of traditional healers "Ferraga" in infants, Morocco

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Background: The "Ferraga" is a traditional children's healer who provides different treatments for various diseases. The practice is based on the application of abdominal scars, points of light and the administration of oral mixtures (cade oil, plants, etc.).[1]
Objective: The aim of this work is to reveal the reality of this activity and its impact on child health and to report four cases of severe poisoning occurring in infants due to these illegal practices.
Case series: We report four cases of poisoning occurring in four infants whose ages were 3 weeks, 1, 4, and 6 months. For therapeutic purposes, the traditional healer gave the children varying mixtures composed mainly of Juniper tar, *Peganum harmala* L, and *Nigella damascena* L. Neurological symptoms occurred in the four infants with coma and convulsions. Two of them had, in addition, respiratory distress and gastrointestinal symptoms such as vomiting, diarrhea, and abdominal pain. Laboratory analysis showed electrolyte disorders, renal and hepatic failure in two infants. The evolution was marked by the deaths of two children (2 days and 1 week after admission); the other two have recovered after symptomatic treatment with discharge after a week of hospitalization. All etiological investigations were negative, so toxic origin was considered for the four cases and the *Peganum harmala* alkaloids were identified in the sample mixture administered by the traditional healer.
Conclusion: Traditional healing is a widespread activity in Morocco. It exposes patients to a risk of poisoning and could compromise the life of many innocent people, with significant morbidity and mortality.

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214. Fatal poisoning due to Indigofera

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Objective: Indigo, also known in Morocco as Nila, is a dye widely used in the coloring of Moroccan handicrafts. It is obtained from fermentation reactions on the leaves and branches of true indigo, *Indigofera tinctoria*, which is a widespread plant in tropical Africa and Asia.[1] We report a case of fatal poisoning in a 3-year-old child after administration of indigo for therapeutic purposes.
Case report: A child of 3 years without medical history was admitted to the emergency department for consciousness disorders 12h after ingestion of an indeterminate amount of Nila, given by his mother as an antiseptic to treat gastroenteritis. On admission, the child was unconscious (GCS 10), hypothermic, tachycardic 170 beats/min with perioral cyanosis, blood pressure at 70/40 mmHg, prolonged capillary refill time, and oliguria 0.2 mL/kg/h. Abdominal examination revealed a very low peristalsis. Four hours after admission, the child had presented convulsions with hemodynamic disorder requiring intubation and ventilation and treating with macromolecules and vasoactive drugs. Toxicological analyses in the blood and urine was negative. Biological tests demonstrated renal failure, leukoneutropenia, prothrombin time at 30%, hepatic cytolysis, and a CPK MB at 319 U/L. Electrocardiogram revealed diffuse repolarization disorder. The child was treated with N-acetylcysteine to improve hepatic function. All etiological investigations were negative, so toxic origin of Nila administration was retained as diagnosis. Death resulted from multiple organ failure.
Conclusion: The use of indigo in traditional medicine may be responsible for serious accidents or death. Toxicological studies are needed to determine its toxicity in humans and animals.[2]

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215. Neurological toxicity of Nigella

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Objective: Nigella is one of the plants most used in traditional medicine for prophylactic and therapeutic reasons.[1,2] We report a case of poisoning by Nigella in a woman who presented with consciousness disorders and unexplained neurological and radiological lesions of the basal ganglia.
Case report: A 47-year-old woman with no medical history was found unconscious at home and was admitted to the emergency room 2 hours later. Interrogation of the family eliminated any context of carbon monoxide poisoning, alcoholism, addiction, or drug poisoning. At admission, the patient was febrile, hemodynamically stable but unconscious (Glasgow coma scale [GCS], 6) with a bilateral miosis, without meningeal rigidity or neurological deficit. Laboratory tests showed renal failure (urea = 1.05 g/L, creatinine = 26 mg/L) with hyponatremia at 124 mEq/L. Toxicological screening (drugs, medications, and pesticides) was negative in the blood and

urine. Considering the persistence of the consciousness disorder after correction of electrolyte disturbances, a brain scan was performed and revealed bilateral hypodensity of the basal ganglia. Brain magnetic resonance imaging found a bipallidal hypersignal on T2 without abnormalities of the white substance or cerebral atrophy. Progressive improvement in consciousness occurred after 10 days. The patient confessed to the ingestion of ground Nigella seeds for dysphonia resistant to treatment. Toxicological advice was sought, and a sample of the plant consumed was sent to the National Poison Control Center who identified *Nigella damascena* L. (the most poisonous species of Nigella). The outcome for our patient was favorable after symptomatic treatment,with recovery of consciousness without neurological sequelae. Considering the spontaneously favorable outcome and the absence of other etiology (tumor diseases, vascular, infectious, or inflammatory) explaining the coma with basal ganglia lesion, poisoning of Nigella was retained as the diagnosis.

Conclusion: Poisoning by Nigella may be responsible for serious accidents. Physicians should be aware of this type of poisoning and consider this diagnosis when faced with any unexplained consciousness disorders.

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216. Suicidal *Digitalis purpurea* poisoning treated with specific Fab fragments

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Objective: Foxglove ingestion is a well-known but rarely reported poisoning.[1–4]

Case report: A healthy 52-year-old man ingested five leaves of *Digitalis purpurea* in the evening to commit suicide. He fell asleep, but woke up next morning with nausea, vomiting, and pressure in his chest. On hospital admission a few hours later he had normal blood pressure and respiratory rate. Routine laboratories, including s-potassium and s-creatinine, were normal. S-digoxin was 0.3 nmol/L (therapy: 1.5–2.6). Electrocardiography (ECG) displayed bradycardia, 30/min and AV block I. During the following hours, cardiac monitoring revealed episodes of sinus arrest and asystolic pauses up to 6 seconds. The arrests were managed with atropine, but in the afternoon, the frequency of asystolic episodes increased. Twenty-four hours after ingestion, four vials (160 mg) of digoxin-specific Fab fragments were administered. During the 12 hours after the antidote treatment there were no asystolic episodes but bradycardia remained. A new s-digoxin showed 0.7 nmol/L. New episodes of sinus arrest up to 6–7 seconds were noted 36 hours after ingestion; therefore, two more antidote vials were given. Again, this eliminated the arrests. During the following six days, the ECG remained pathologic with bradycardia and sinus arrests of 3–5 seconds. Blood sample for s-digitoxin was not taken until six days after ingestion when it displayed 23 nmol/L (therapy: 10–40). The patient was discharged after nine days with a normal ECG.

Conclusion: *Digitalis purpurea* does not contain digoxin, but digitoxin and other toxic glycosides.[1,3] However, glycosides from *D. purpurea* cross-react with commonly used digoxin immunoassays.[3] Two leaves of *D. purpurea* are potentially lethal and ingestion of a whole plant has been rapidly fatal despite adequate antidote treatment.[3,4] Prolonged ECG disturbances are typical in non-fatal cases.[1,2] The efficacy of specific Fab fragments is not fully established.

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217. Severe poisoning with "Maâjoun": A case report

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Objective: Maâjoun is a paste traditionally prepared with cannabis, with hallucinogenic plants such as the seeds of Datura, the leaves of Belladonna, and sometimes psychotropic medication especially benzodiazepines added. In Morocco, Maâjoun is consumed as an aphrodisiac or an addictive substance.[1,2] Poisoning is usually the result of an overdose.[1,2] We report a case of severe poisoning with Maâjoun with favorable outcome after symptomatic treatment.

Case report: A 21-year-old man without medical history was admitted to the emergency department for agitation and unexplained consciousness disorder. The history of the symptoms went back to the day before his admission. The patient had consumed at a party a suspect product having the appearance of a chocolate. One hour later, the patient developed vomiting, headache, and high fever with stiffness in his joints. Clinical examination found an unconscious patient with a Glasgow coma scale (GCS) score of 10, red conjunctiva with spontaneous tearing, hyperthermia at 41°C, and tachypnea at 40 cycle/min. The rest of the clinical examination was normal. Laboratory tests, a lumbar puncture, and a brain scan were normal. Testing his urine found the presence of a metabolite of cannabis (tetrahydrocannabinol THC) and benzodiazepines, and these two molecules were quantified showing a high concentration of tetrahydrocannabinol (205 ng/L) and benzodiazepines (3100.80 mg/L). Complementary analysis using high-performance liquid chromatography with diode barrette (HPLC/DAD) confirmed the presence of metabolites of cannabis, diazepam, and clorazepate

dipotassium in the serum and urine. The patient recovered favorably after a week of hospitalization in the intensive care unit.
Conclusion: Poisoning with Maâjoun is usually mild; however, in case of overdose, intoxication can be fatal for addicts.[3]

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218. *Echinoderma asperum*: *In vivo*, acetaldehyde-syndrome after consumption together with alcohol (case series); *in vitro*, suppression of acetaldehyde-dehydrogenase activity

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Objective: A Coprinus-like syndrome after co-consumption of the mushroom *Echinoderma asperum* (Ea) with ethanol is known from a small case series.[1] Aldehyde dehydrogenase(ALDH)inhibition can be hypothesized as a possible pathomechanism. With the multicenter- GfkT-database ProPi, we identified three additional cases in Switzerland, Thuringia, and Bavaria. These new cases gave reason to test this hypothesis *in vitro*.
Case series: Each of the cases had a well-stewed meal of self-collected mushrooms, identified later as Ea by certified mycologists. None had eaten other mushrooms or taken ALDH-inhibiting substances. A single alcoholic beverage up to 4 hours after the meal precipitated symptoms within 15 minutes: throbbing headache, tightness of the chest, dyspnea, and flushing of the head with burning sensation; two cases vomited, and one case had diarrhoea after 60 min. The symptoms disappeared within 3–12 hours of observation.
Method: Experimental: Ea specimens from the Bavarian case and *Agaricus bisporus* and *Pleurotus ostreatus* as controls were tested in an ALDH assay, modified from Maninang et al[2]: ALDH (yeast, Sigma) 1887 U/L Trispuffer pH 8.0 K 0.1 M, KCl 0.1 M, acetaldehyde 5.5 mM reacted with NADH 20 mM in 300-µL multiplate reaction wells with and without addition of 10, 30 and 50 µL mushroom sap. NADH formation was monitored by UV absorption at 340 nm. Saps were obtained after thawing the deep-frozen mushrooms.
Results: Thirty and 50 µl sap from Ea inhibited ALDH completely, and 10 µL stopped NADH formation at 25% of controls. *Agaricus bisporus* and *Pleurotus ostreatus* caused no inhibition.
Conclusion: *Echinoderma asperum* inhibits ALDH. With a multicenter database, we identified additional human cases of acetaldehyde syndrome after co-consumption of Ea with alcohol. The toxin is not yet identified. Further investigations are in progress.

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219. Aggressive treatment results in complete resolution of *Amanita bisporigera* toxicity

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Background: Ingestion of Amanita mushrooms continues to result in significant morbidity and mortality worldwide. Treatment options include multiple doses of activated charcoal; N-acetylcysteine; high-dose penicillin G; silimarin, and even biliary drainage and octreotide. In the United States, silimarin (Legalon® SIL) has recently received Food and Drug Administration (FDA) orphan drug status and can be administered to patients with suspected Amanita poisoning. We describe a case of Amanita poisoning with a successful outcome due to aggressive treatment and collaborative efforts among numerous healthcare providers.
Case report: A 65-year-old male presented to the emergency department (ED) with complaints of persistent vomiting and diarrhea which began 14 hours after ingesting mushrooms he foraged from his yard. He was hemodynamically stable and had an unremarkable physical examination. Intravenous fluids, antiemetics, and a proton pump inhibitor were initiated. Initial abnormal laboratory results included aspartate aminotransferase (AST)192 U/L and alanine aminotransferase (ALT) of 144 U/L. The mushrooms were available and photographed in the ED. By communication with the Poison Center, a mycologist positively identified the mushrooms as *Amanita bisporigera*. N-acetylcysteine was started. Immediate contact with the pharmaceutical company led to the release of Legalon® SIL which was initiated 18 hours after presentation. On hospital day 2, AST and ALT peaked at 5102 U/L and 2546 U/L, respectively, and INR peaked at 1.9. Biliary drainage was placed and octreotide was administered. On hospital day 6, liver enzymes were declining and less than 1000 U/L, and N-acetylcysteine and Legalon® SIL was discontinued. The patient was discharged to home on hospital day 8 with anticipated full recovery.
Discussion: Unintentional poisoning from Amanita mushrooms most often results from foraging errors and misidentification. Presentation to health care is often delayed due to the late onset of toxic effects. Administration of Legalon® SIL within the first 48 hours dramatically decreases mortality and has changed the way we manage these patients. Until this drug is readily available and FDA-approved, there is a delay in administration.
Conclusion: Rapid recognition and early consultation with a poison center will help expedite aggressive care, including Legalon® SIL, and may result in improved outcomes.

220. When folk medicine harms: Four pediatric cases following ingestion of *Laurus nobilis* infusion

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Objective: *Laurus nobilis* is an evergreen plant, commonly known as Laurel or Bay-tree, growing wild along the Northern shores of the Mediterranean Sea. In popular Italian tradition, the Laurel has a wide therapeutic use: the extracts appear to possess digestive, antispasmodic, antiseptic, expectorant, diuretic, emmenagogue, and antirheumatic properties. The leaves are used to add flavor to food and to make infusions, syrups, and liqueurs. They are exploited in Iranian traditional medicine to treat epilepsy, neuropathy, Parkinsonism, hemorrhoids, and mycosis. In Italy, above all in Sicily, it is given to infants, because it is credited to relieve colic. We describe four cases of *Laurus nobilis* intoxication in pediatric patients.
Case series: Four pediatric cases came to the attention of Pavia Poison Center. Case 1: A 2.5-month-old infant was given a daily dose of highly concentrated Laurel decoction for 2 weeks. He presented with regurgitation, drooling, vomiting, tremors, muscle laxity in the head, and irritability. Case 2: A Sicilian grandmother gave her 15-day-old grandchild Laurel infusion. He became hyporeactive, hypotonic, and necessitated immediate admittance to the emergency department. Case 3: A 4-month-old infant presented with regurgitation, difficulty in breathing, hyporeactivity after ingesting a Laurel infusion for colic. Case 4: An infusion of Laurel caused lethargy in a 45-day-old infant. All the 4 cases were resolved after a short period of clinical observation, without giving any specific pharmacological therapy.
Conclusion: The main component of the Laurel leaves is an essential oil comprising cineol, linalool, geraniol, eugenol, methyleugenol, phellandrene, apinene, and eucalyptol. These molecules are responsible for the side effects. Because of their low molecular weight, volatility at room-temperature, lipophilia, they can cross the blood–brain barrier, giving rise to a confusional state and neurological disorders. Pharmacological studies demonstrate the anesthetic, muscle-relaxant, anticonvulsant, and thus, central nervous system (CNS) depressant activity of cineol, linalool, eugenol, and methyleugenol, which, at high concentrations, can cause drowsiness and dyskinesias. According to recent literature, underlying the CNS depressant action of the terpenes of Laurel is the modulation of glutamatergic and GABAergic neurotransmission. An infusion of Laurel should not be administered in infancy: there are no evident beneficial effects and a definite toxicological risk.

221. Poisonings with alkaloids of Veratrum in Russia

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Objective: Veratrine poisonings occasionally happen in Europe.[1] Hellebore is used in Russia in veterinary medicine as an emetic. Some people consume hellebore tincture as cheap alcohol. Sometimes housewives, who are extremely tired of their husbands' alcoholism, stir it in alcohol, in order to make them drop this habit. This hardly ever rescues people from alcoholism, but may cause severe poisoning.
Methods: A retrospective study of all cases of acute veratrine poisoning over 10 years (2003–2012) was carried out in 4 poisoning treatment centers in the cities Yekaterinburg, Tyumen, Chelyabinsk, and Irkutsk. Veratrine was identified in urine using gas chromatography–mass spectrometry (GC–MS) or thin-layer chromatography in all cases. Six hundred and sixty-eight cases were included in the study.
Results: Veratrine poisoning varied from 0.3% of hospitalized cases of acute poisonings in Irkutsk to 1.5 in Tyumen, 1.7% in Chelyabinsk, and 2.2% in Yekaterinburg. The majority of patients were men—from 65% in Irkutsk to 87% in Yekaterinburg. Clinical features were weakness, sweating, nausea, vomiting, hypotension, and slow heart rhythm in all cases. Consciousness disorders appeared in 44% of patients in Irkutsk but only in 7% for Yekaterinburg. The main electrocardiographic (ECG) findings were atrio-ventricular block of first degree in 7.1–13%, second degree in 5.6–8.6% and early repolarization syndrome in 15.6–24.1% of cases in different poison centers. One patient developed acute renal failure due to a long period of hypotension before admission and was treated with conventional hemodialysis for 26 days. There were 2 deaths: the first, a 28-year-old woman who ingested a hellebore root decoction and was found unresponsive after 7 hours; the second, a 68-year-old man who had ingested 100 mL of hellebore extract. He had a history of tuberculosis and chronic heart failure.
Conclusion: Veratrine acute poisoning is widespread in Russia. It causes cardiotoxic effects and rarely death.

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222. Biological and botanical confirmation of solanaceous glycoalkaloid poisoning by susumber berries (*Solanum torvum*)

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Objective: Sporadic reports of poisoning following ingestion of the Jamaican *Solanum torvum* (susumber or turkey berry) are characterized by varying degrees of cranial nerve abnormalities, rhabdomyolysis, gastrointestinal symptoms, and peripheral and respiratory

weakness. Solanaceous glycoalkaloids are the putative causative agents. We report a case of susumber poisoning with cranial nerve weakness and peripheral neuropathy with biological and botanical confirmation.

Case report: A 54-year-old woman, 84 kg, boiled susumber berries transported by a friend from Jamaica and ate "a lot." Her family ate less, dissuaded by the berries' characteristic bitterness. She woke the following morning, noting difficulty focusing vision, dysarthria, decreased left-hand sensation, and gait instability. Following emergency medical service transport, her triage vital signs were blood pressure, 168/88 mmHg; heart rate, 83/min; respiratory rate, 15/min; temperature, 36.7ºC; pulse oximetry, 95%; and glucose, 5.3 mmol/L. She reported tongue "heaviness" and diffuse myalgias. Her physical examination was significant for miosis, opsoclonus, severe dysarthria, dysmetria, and mild upper and lower extremity weakness and tenderness. Laboratory analysis revealed an abnormal peak serum creatine phosphokinase, 1886 IU/L. Brain magnetic resonance imaging (MRI) revealed no ischemic lesions. A lumbar puncture revealed: opening pressure, 29 mmH_2O and normal cerebrospinal fluid (CSF) cell counts, protein, and glucose. She was hospitalized to monitor her respiratory status, although she required no intervention. Her neurological deficits resolved with supportive care, and she was discharged home on hospital day (HD) #3. Her serum and berries from the same batch that she prepared were analyzed. Using high-resolution, mass accuracy mass spectrometry technology (Orbitrap, ThermoFisher), we identified a range of solanaceous glycoalkaloids (solanine, chaconine, solasonine, solamargine, dioscin, and tomatin) and associated free alkaloids (solanidine, solasodin, diosgenine, and tomatidine) in the toxic berries, but not in commercially sold, edible samples. Interestingly, solanidine and solasodin were identified in the patient's serum on HD #1, but not subsequently.

Conclusion: Susumber toxicity with neurological deficits and rhabdomyolysis followed consumption of noncommercial susumber berries. Glycoalkaloids in poisonous berries were absent in commercial berries. Toxic alkaloids solanidine and solasodin were identified in the patient's admission serum specimen, but cleared rapidly, consistent with the patient's rapid recovery. These data suggest a potential prognostic and confirmation screening mechanism for susumber poisoning.

223. The management of ventricular dysrhythmia in aconite poisoning: A review of published cases

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Objective: Aconite toxicity is frequently complicated by ventricular dysrhythmia. The current advice cited on TOXBASE® is to "treat arrhythmias conventionally."[1] This study reviewed the published clinical evidence in order to rationalize the management of aconite-induced ventricular dysrhythmia.

Method: A review of the English literature was conducted using the search terms "aconite," "aconite + poisoning," and "aconite + dysrhythmia".

Results: Forty cases of probable aconite-induced ventricular dysrhythmia were identified (Table 1).

Conclusion: Consideration should be given to the following: early administration of bicarbonate in the presence of ECG changes; a role for class 1c agents, ideally flecainide, if there is no history of structural heart disease; the importance of prolonged resuscitation.

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Table 1. Reported cases of aconite-induced ventricular dysrythmia.

Number of patients	Timing of the onset of symptoms (minutes)	Dysrythmia	Treatments	Outcome	Reference
2	10	VT(2)	Amiodarone + cardioversion (1), amiodarone + Mg^{2+} (1)	Died (1) Survived (1)	2
1	60	VT	Lidocaine then amiodarone	Survived	3
1	90	SVT then VT then PEA	Cardioversion + "various pharmacological agents" + prolonged CPR	Survived	4
1 with reporting of a further 4	20	Ventricular ectopics (1), VT (4)	Mg^{2+} + cardioversion (1), flecainide (1), amiodarone (2), lidocaine (1)	Survived (5)	5
17	–	VT (13), VF (2), ventricular ectopics (2)	Lidocaine (10), amiodarone (5), flecainide (2), procainamide (1), mexiletine (1). Prolonged CPR (7)	Survived (15), Died (2)	6
14	–	VT (12), ectopics (2)	Lidocaine (4), amiodarone (5), flecainide (2), procainamide (1), mexiletine (1).	Survived (14)	7

CPR = cardio-pulmonary resuscitation, VT = ventricular tachycardia, VF = ventricular fibrillation.

224. The use of plants and media vigilance

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Background: According to its culture and beliefs, the Moroccan population uses plants for therapeutic purposes, cosmetics, and others. This use is encouraged by the messages delivered by the media often by non-specialists.
Objective: To assess the danger of radio programs concerning the promotion of plants on the health of the population.
Methods: A retrospective study of poisoning cases by plants received by the Moroccan Poison Control Center (MPCC) by phone during May 2013 and analysis of different messages broadcast by the media to the general population for the promotion of plant use.
Results: Five cases of serious adverse effects of plants were detected. These so-called "medicinal" plants were consumed by persons who heeded advice on the radio on their therapeutic and beneficial effects. The adverse effects were respiratory distress and coma after ingestion of *Anacyclus pyrethrum*; inflammation of face after application of *Citrus aurantium* L.; hepatic cytolysis secondary to *Euphorbia resinifera* Berg; priapism and dark urine after *Haplophyllum vermiculare* Hand and *Rosmarinus officinalis*; and cardiac arrest after use of oil of *Artemisia herbaalba* Asso. The analysis of different messages broadcast by the media to the population has shown some breaches.[1,2] The MPCC reacted by triggering an alert to the Ministry of Health who alerted the High Authority of Audiovisual Communication (HACA). In addition, the MPCC responded with messages and programs on radio and television to educate the general population on the risks associated with the use of plants advised by the media.
Conclusion: Instead of encouraging these practices, the media should be involved in awareness and education of the population against uncontrolled use of plants.

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225. Adverse effects due to the use of medicinal plants in the Moroccan diabetic

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Table 1. Adverse effects and responsible plants, survey in diabetics, Morocco, 2013.

Adverse effects according WHO ART	Plants involved	Frequency	%
Gastrointestinal system disorders	Mixture of plants	16 cases	66.6
Body as a whole-general disorders	*Trigonella foenum-graecum* and/or *Salvia officinalis*	3 cases	12.5
Urinary system disorders	*Juglans regia* L. and/or Mixture of plants	3 cases	12.5
Cardiovascular, general	*Trigonella foenum*	2 cases	8.3
Total		24 cases	100

Background: Diabetes is a public health problem in Morocco. The prevalence in 2000 was 6.6%.[1] The use of plants to treat diabetes has become increasingly important, encouraged by some international studies.[2]
Objective: The objective of this study was to detect plants frequently used by diabetics and to identify those implicated in adverse reactions.
Methods: A survey was conducted using a questionnaire on the use of medicinal plants by diabetic patients belonging to 2 associations for diabetics and diabetic consultants in six health centers in the studied region.
Results: Among the 350 field questionnaires, 210 were analyzed. It appears from the analysis of these questionnaires that 57% of diabetics used medicinal plants to treat their diabetes: 4% exclusively, 88% in conjunction with their medical treatment, and 8% used plants irregularly with their medical treatment. Among the 119 diabetics who used plants, 24 have had adverse effects (20%). The most commonly implicated plants and their adverse effects are mentioned in Table 1.
Conclusion: The use of medicinal plants is very common in the management of diabetes in Morocco. Adverse effects due to these plants are not negligible.

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226. Paracetamol excess related to dental pain in adults: National Poisons Information Service enquiries pre- and post-Medicines and Healthcare Products Regulatory Agency guideline changes

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Table 1. Dental paracetamol enquiries to the NPIS pre- and post-MHRA guidance change.

	2011–12		2012–13	
	No.	%	No.	%
NPIS calls: all enquiries	46,671		52,223	
NPIS calls: paracetamol	5,748	12.3%	7,841	15.0%
NPIS calls: unintentional paracetamol exposures	3,035		5,221	
Paracetamol exposures relating to dental pain	587	1.3%	1449	2.8% ($p < 0.0001$ compared to pre-change)
Referred to the emergency department	243	41.4%	911	62.9% ($p < 0.0001$ compared to pre-change)
NPIS Treatment recommendation given	343	58.4%	1076	74.3%
NPIS Treatment recommendation recorded:	129		400	
Referred to an NPIS physician	8	6.2%	83	20.8%
Investigations	86	66.4%	259	64.8%
Antidote	78	60.5%	112	28.0%

Objective: Paracetamol enquiries comprise 12–15% of National Poisons Information Service (NPIS) call volume, of which 10–18% relate to dental pain. Recent changes in the guidance from Medicines and Healthcare Products Regulatory Agency (MHRA) for paracetamol poisoning included the removal of "risk factors" from patient assessment and lowering of the nomogram treatment line from 200 to 100 mg/L at 4 hours. We aimed to examine the impact of MHRA changes to treatment guidance on enquiries about accidental paracetamol excess in the context of dental pain.

Methods: Calls involving paracetamol were extracted from the UK Poisons Information Database (UKPID) for 1 year before and 1 year after the management change (3/9/2011 to 2/9/2013). Enquiries were selected based on keywords "tooth," "dental," "dentist," or "teeth" and analysed in a Microsoft Access database.

Results: See Table 1. Examining the data by month revealed 3 periods: a pre-change baseline (49 enquiries/month), a four-month immediate post-change period (221 enquiries/month), and a post–change return to new baseline (71 enquiries/month).

Conclusion: The new MHRA guidance resulted in a major increase in calls to the NPIS and in referrals to hospital relating to excess paracetamol ingestion for dental pain.

227. Prolonged, intermittent Brugada after imipramine overdose

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Objective: To described a case of imipramine overdose causing a Brugada-like pattern on electrocardiogram (ECG).

Case report: A 48-year-old woman with a past medical history of depression was transported to an outside emergency department following an overdose of imipramine and gabapentin. She was endotracheally intubated for airway protection. The initial QRS was 152 ms, and she was given two ampules of sodium bicarbonate and started on a bicarbonate infusion at 100 cc/hr. Her QRS improved to 144 ms, and she was transferred to a tertiary care intensive care unit (ICU). Upon arrival, vital signs were heart rate 89 beats/min, blood pressure 100/80 mmHg, and respiratory rate 14 breaths/min. ECG on arrival demonstrated QRS 128 ms and QTc 571 ms. Physical examination was remarkable for myoclonic jerk, hyperreflexia, and sustained clonus. Arterial blood gas has pH 7.7, pCO_2 26 mmHg, and calculated bicarbonate 34 mEq/L. Sodium bicarbonate infusion was titrated for a pH 7.45–55, which was continued until hospital day (HD) 5. An electroencephalogram (EEG) performed revealed no epileptiform activity. On HD 2, the patient's ECG revealed a Brugada pattern, which resolved completely on HD five. Urine gas chromatography/mass spectrometry drug screen showed imipramine, midazolam, propofol, ibuprofen, caffeine, diphenhydramine, venlafaxine, atenolol, mirtazapine, buclizine, hydroxyzine, and trazodone. The patient had no prior history of Brugada Syndrome. Of note, the patient presented again 3 months later following a polysubstance overdose consisting of imipramine, alprazolam, zolpidem, quetiapine, trazodone, and venlafaxine. There was no Brugada pattern noted on ECG during that admission. Her QRS was 150 msec, necessitating bicarbonate therapy and recovered.

Conclusion: A Brugada pattern is seen in less than 3% of tricyclic antidepressant overdoses. Brugada syndrome is associated with mutations in the sodium ion channel with several ECG patterns, characterized by incomplete right bundle branch block and ST elevations in the anterior precordial leads. This pattern may be intermittent and persistent despite bicarbonate therapy. Imipramine toxicity can cause ECG abnormalities similar to those of Brugada syndrome. Treatment is centered on meticulous supportive care and sodium bicarbonate administration until toxicity resolves. Physicians should be aware of this unusual clinical presentation.

228. Rate dependent bundle branch block in drug overdose: A case report

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Objective: To describe a case of rate-dependent bundle branch block (RDBBB) in an overdose of desvenlafaxine and temazepam.

Case report: A previously healthy 21-year-old male presented by ambulance 3 hours after an overdose of 2.35 g (47x50 mg) desvenlafaxine and 250 mg (25x10 mg) temazepam. His Glasgow coma score was 7 and normotensive with a heart rate (HR) of 145 bpm. His first electrocardiogram (ECG) showed sinus tachycardia of 152 bpm with normal QRS and QT intervals. One hour later, the patient developed a left bundle branch–type block pattern with a HR of 138 bpm. This persisted for 4 hours after which the conduction delay reverted back to a normal QRS morphology and duration with a HR of 123 bpm. The patient remained haemodynamically stable throughout and made an uneventful recovery. Six weeks later the patient underwent an exercise stress test to further study possible

mechanisms for his ECG abnormality. Despite achieving a HR of 185 bpm, his QRS morphology remained normal with no ischaemic changes.

Conclusion: RDBBB was first described in 1913[1] and was thought to be secondary to ischaemic heart disease but has been demonstrated in patients with normal coronary angiography.[2] In overdose it has only been reported with amisulpride.[3] Postulated mechanisms include an alteration in the his-Purkinje system cycle length—refractory period relationship whereby the refractory period duration becomes relatively longer than the cycle length, which shortens with increasing HR. This finding is morphologically distinct from the QRS widening seen with sodium channel blocking drugs, for example, tricyclic antidepressants. It is unknown whether drug-induced RDBBB occurs simply because of a drug-induced tachycardia, or if other drug-related mechanisms are also contributing in a patient with underlying propensity to develop RDBBB.

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229. Serotonin syndrome in tramadol overdose patients

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Objective: Tramadol overdose and abuse is rather common in Iran. Because of its analgesic properties, it is a medication frequently abused.[1] It has been shown that tramadol overdose can induce serotonin syndrome (SS), and SS has been known as an adverse side effect of serotonergic agents since 1960. Clinical features can be varied from very mild to fatal.[2]

Methods: In this study, patients who were admitted because of tramadol overdoses to Imam Reza (p) Hospital from September 21,2011 to January 21,2012 were recruited. Clinical findings were recorded every 6 hours in the first 24 hours of admission. SS was determined based on Hunter Criteria (HC) if one of the following happened: spontaneous clonus; inducible clonus plus agitation or diaphoresis; ocular clonus plus agitation or diaphoresis; tremor and hyperreflexia; hypertonia; and temperature above 38°C plus ocular clonus or inducible clonus.[3]

Results: In total, 5 patients developed SS when HC was taken into account. Three of them presented with spontaneous clonus, hyperreflexia, and tremor. One of them presented with spontaneous clonus plus diaphoresis and another presented with spontaneous clonus, hyperreflexia, tremor, and diaphoresis. Patients were managed with fluids, activated charcoal, supplemental oxygen, gastric lavage, naloxone (if needed), and diazepam to control agitation or seizures and management of other signs and symptoms when they happened. Cyproheptadine (4 mg every 8 hours) was also administered to patients.

Conclusion: As there have been a number of incidents of SS in tramadol overdose patients in our area, we recommend further studies to develop an approach to prevent SS in tramadol overdose patients.

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230. Polypharmacy reported by emergency department patients presenting with psychiatric crises

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Objective: To determine the extent of polypharmacy reported by psychiatric patients presenting to an emergency department with psychiatric crises.

Methods: A prospective observational pilot study of self-reported psychotropic medication use was conducted in emergency patients (ED) presenting with psychiatric complaints. Inclusion criteria were age greater than 17 years, emergency department admission for a psychiatric visit, and ability to obtain informed consent from the patient or authorized representative. Enrollment was conducted in June and July of 2013. A study investigator interviewed patients regarding previous psychiatric diagnoses, previous and current psychotropic drug prescriptions, chief complaint, and medical and surgical histories. Psychiatric history and prescriptions were verified by review of medical and pharmacy records whenever available. Descriptive statistics are reported with comparisons between polypharmacy and other patients.

Results: Seventy-six patients were enrolled in this study. Ten patients who were not currently taking psychotropic drugs were excluded from the analysis presented here. Of the 66 patients included in this analysis, 83.3% (55) of the patients were taking two or more psychiatric medicines and 50% (33) were on three or more; 50% (33) of patients were taking more than one drug in the same class, and 72.7% (48) of patients were taking drugs from more than one class. Among patients who were on three or more psychiatric medications, the most common chief complaint or reason for presentation to the ED was suicidal/homicidal ideations (42.4%, $n = 14$), and the number of psychiatric diagnoses ranged from 1 to 6 (median = 2). These were not significantly different from patients on fewer than three meds. Patients on three or more drugs were more likely to be on antipsychotics than patients on fewer than three ($p = 0.008$), and 16.7% (11) of these patients were on at least 2 antipsychotics.

Conclusion: Psychiatric polypharmacy is reported among patients with crises, often taking drugs with potentially dangerous overlapping mechanisms of action. These patients continue to have psychiatric crises needing ED care. Either polypharmacy does not prevent crises

or there is non-compliance. This preliminary investigation suggests further investigations with laboratory verification of drug use.

231. Human exposures to non-opioid analgesics reported to the Poisons Information Centre Erfurt from 2003 to 2012

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Objective: The aim of the study was to obtain recent information on important characteristics of all human exposures to non-opioid analgesics (NOP) reported to the Poisons Information Centre (PIC) Erfurt over a 10-year period.
Methods: In a retrospective study, we analysed the change in frequencies, circumstances of exposure, symptom severity, age groups, and substances involved in all NOP-related enquiries to the PIC Erfurt from the beginning of 2003 to the end of 2012.
Results: In total, 8,405 cases of NOP exposures with 15,528 NOPs were registered. In 4,749 cases, only one NOP was involved. Although the cases of NOP exposure increased almost twofold from 635 in 2003 to 1,002 in 2012 their relative frequency compared to all cases of exposure remained almost constant at 6.4% (6.0–6.7%) over the same period. Paracetamol exposures increased from 424 in 2003 to 579 in 2009 and then fell to 445 in 2012. Ibuprofen exposures, however, continuously increased from 228 in 2003 to 762 in 2012. Age groups involved in NOP exposures were more often adults 67.1% and less frequently children 32.7% (toddlers 15.7%) than in all exposures (adults, 48.7%; children, 48.7%; (toddlers, 34.2%)). The proportion of suicidal exposures was higher in NOP exposures (57.6%) than in all exposures (23.6%), whereas the proportion of accidental exposures was lower (NOP exposures: 21.5%, all exposures: 59.3%). The ten most frequent NOPs in monoexposures were paracetamol (n = 1,686), ibuprofen (n = 1,439), and acetylsalicylic acid (n = 456), dipyrone (n = 274), diclofenac (n = 267), flupirtine (n = 138), naproxen (n = 41), etoricoxib (n = 36), indomethacin (n = 24), and dexketoprofen (n = 19). NOP exposures resulted mostly in none to mild symptoms (77.0%) and rarely in moderate (2.1%) or even severe symptoms (1%). There was only one death, involving the suicidal ingestion of 32 g acetylsalicylic acid by an adult.
Conclusion: NOPs are involved in almost one-tenth of all human poisonings and one-fifth of all human drug exposures. Because many NOPs are over-the-counter drugs, it is difficult to obtain data on their use. Although PIC data are not obtained by a cross-sectional study, they may provide additional information on the risk of their use in the respective populations.

232. Injection of crushed tablets: A prospective observational study

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Objective: Inquiries to the Swedish Poison Centre regarding intravenous injection of crushed tablets are common. Severe complications such as pulmonary granulomatosis after long-term use are described in the literature, but knowledge of the acute toxicity is limited.[1] Hence, the aim of this study was to collect information about acute symptoms after intravenous injection of tablets.
Method: All inquiries to the center regarding intravenous injection of tablets during a two and a half-year period (January 2011–June 2013) were included. When available, full case records from hospitals were collected and analyzed.
Results: There were 120 inquiries regarding intravenous injection of tablets during the study period. In 85 of these, full case records were obtained and constituted the final study material. The majority of patients were males (n = 55), and the age varied between 16 and 54 years. In 74 of the cases (87%), drug abuse was known and in 40 (47%) multiple drugs had been injected. The most common substances were methylphenidate (47%), buprenorphine (19%), and other opioids (18%). In about three-quarters of the cases, the acute clinical symptoms correlated well with the effects of the injected substance. Minor local symptoms at the injection site were noted in 12 cases. Fever developed in 25 patients, 6 of whom had high C-reactive protein values indicating infection. In one patient, severe complications occurred. She developed disseminated intravascular coagulation (DIC), hemolytic anaemia, and renal failure. Most of the patients were discharged after 12–24 hours. Long-term follow-up was not possible.
Conclusion: This study shows that injected crushed tablets give rise to acute symptoms mainly related to the substances used. In addition, fever seems to be a common clinical feature, probably because of pyrogenic reactions triggered by non sterile solutions, a direct symptom of the injected substance, or because of sepsis. Only one case with severe symptoms necessitating prolonged hospitalization was observed, indicating that serious acute complications are rare but they occur. Since long-term follow-up was not possible, development of later complications cannot be excluded.

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233. Cardiomyopathy caused by naphazoline

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Objective: Takotsubo cardiomyopathy is a cardiomyopathy characterized by acute reversible apical ventricular dysfunction and apical akinesis in the absence of obstructive coronary artery disease. We describe a case of Takotsubo cardiomyopathy caused by naphazoline.
Case report: A septumplasty surgery was conducted in a 28-year-old patient. A 0.1% naphazoline solution was prescribed postoperative as decongestant therapy. Eleven days after surgery he got a new bottle of the solution as an extemporaneous mixture from the pharmacy. Some minutes after application of 2 mL of the new solution, the patient complained of nausea, vomiting, sweating, and reduced consciousness. His heart rate was 40/min with a

systolic blood pressure of 200 mmHg on arrival in the ear, nose, and throat (ENT) department. After it turned out that the solution erroneously contained 10% naphazoline, the poisons center was called and the patient was transferred to the department of internal medicine. There the patient felt well, and physical examination including electrocardiogram (ECG) was unremarkable. Blood results revealed slightly elevated troponin level (0.68 ng/mL). A left cardiac catheterization on day 2 after admission showed slight apical hypokinesia without coronary macroangiopathy. In the angiography, this looked "similar to healing Takotsubo cardiomyopathy", and treatment was started with low-dose bisoprolol and ramipril. The further course was unremarkable. Echocardiography 4 days after admission showed normal cardiac function.

Conclusion: A major factor in pathogenesis of Takotsubo cardiomyopathy (broken heart syndrome, stress induced cardiomyopathy) is a catecholamine surge. Because naphazoline is an agonist on alpha receptors, it seems plausible that it can cause this kind of cardiomyopathy after application of high doses. The authors found no report of this complication in the Medline database.

234. Clinical findings and genomic biomarkers in three cases of chronic ciguatera poisoning

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Objective: Chronic ciguatera (CC) poisoning is reported in approximately 5% of acutely poisoned ciguatera patients. Experimental data (mice) demonstrated the activation of anti-inflammatory genes in tissues.[1] We investigated three cases to evaluate the genetic predisposition (HLA-molecular profile), the clinical manifestations, and neuropathological alterations in CC poisoning. A fourth patient, presenting only acute ciguatera, was considered as control.

Methods: All cases were assessed for clinical manifestations, duration, and outcome. Thermal-quantitative sensory tests (QST) and epidermal nerve fiber density (ENFD) with neurodiagnostic skin biopsy were proposed. Genomic typing for HLA-class I/II molecules was performed (PCR-SSP technique).

Results: Three adult Caucasian patients were studied. Case 1: hallucinations, saddle paresthesiae/dysesthesiae, myalgias, asthenia, itching for 8 years (duration of 4–5 months/year, 1st episode 8 months after the acute phase); QST was abnormal and ENFD, compatible with small-fiber neuropathy, was documented. Case 2: itching, paresthesiae/dysesthesiae temperature-related, asthenia, myalgias, and headache 1 month after the acute phase. QST was normal and skin biopsy revealed a minimal ENFD reduction. Case 3: paresthesiae in the hands for 1 year (1 month after the acute phase). QST was positive. Skin biopsy was not performed. All patients had two HLA class I amino acid motifs that are ligands for the inhibitory natural killer cell receptor KIR3DL1 (38.21% in ethnically matched controls), all shared the HLA-DRB1*11,DQB1*03 haplotype (25.8% in controls), 2 carried the entire HLA-B49 haplotype (0.8% in controls) and 2 the HLA-DRB1*04 allele (7.75% in controls). The control case (only acute ciguatera) was completely different, lacking all these biomarkers.

Conclusion: Our results are consistent with those of the single literature report that ascribes to HLA-DRB1*11 and DRB1*04 (serologically defined) a susceptibility genetic trait.[2] A possible role of an HLA-KIR mediation under the chronicity of the disease maybe induced by an excess of inhibition of the innate immune response. In the patient presenting long-lasting CC, small-fiber neuropathy may also be documented (case 1). Two patients (cases 1 and 2) had clinical benefit after mannitol treatment: however, clinical evaluation and treatment of CC remain a medical challenge.

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235. The role of GABA receptors during intoxications with designer drugs: A mechanism-based approach for piperazine derivatives

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Objective: Piperazine derivatives have psychoactive effects and are currently detected in ~20% of all ecstasy tablets. Exposure to piperazine derivatives can also occur via metabolites of prescribed medicines, for example, trazodone. Piperazine derivatives increase brain dopamine and serotonin levels, presumably via effects on neurotransmitter reuptake transporters. Besides the intended effects, this can induce adverse effects like agitation, hallucinations, multiorgan failure, and seizures. The relevance of GABA receptors (GABA-Rs) is illustrated by the beneficial effect on agitation and seizures of GABA-R agonists (benzodiazepines) in the treatment of intoxications with stimulatory drugs. Since GABA-Rs provide a major inhibitory input in the brain, a piperazine-induced antagonistic effect on the function of GABA-Rs could also contribute to the increase in brain catecholamine levels. Therefore, we investigated the effects of 12 piperazine derivatives on GABAA-R function and established a rank-order potency.

Methods: Human $\alpha1\beta2\gamma2$ GABAA-Rs were expressed in *Xenopus oocytes* and the effects of piperazine derivatives on GABAA-R function were investigated using the two-electrode voltage-clamp technique. Tested piperazine derivatives included benzylpiperazine (BZP), methylbenzylpiperazines (2/3MBP), phenylpiperazine (PP), methoxyphenylpiperazines (2/3/4MPP/MeOPP), chlorophenylpiperazines (2/3/4CPP), and fluorophenylpiperazines (4FPP/TFMPP).

Results: Piperazine and its derivatives did not act as GABAA-R agonists. However, in the presence of GABA, all derivatives dose-dependently inhibited the GABA-evoked current. Phenylpiperazines induced a higher maximum inhibition of the GABA-evoked current (62% vs. 46%) compared to benzylpiperazines. Based on the concentration that induced 20% inhibition of the GABA-evoked current (IC20), derivatives were ranked from highest to lowest potency; 2CPP> PP = 4MPP > 3CPP > 3MPP > 4CPP > 2MBP = TFMPP > 3MBP > 2 MPP = 3FPP> BZP > 2,3MPP = PP. The strongest (~75%) and most potent (IC20 = 135 μM) inhibition was induced by 2CPP.
Conclusion: Predicting the potency of new derivatives based on molecular structure, functional groups, and the position of these groups is complicated. However, inhibition of GABA-Rs appears a common mode of action for piperazine derivatives at concentrations that can occur in the brain during intoxications. Consequently, GABAergic input on, for example, dopaminergic neurons is decreased, and this can contribute to increased dopamine and serotonin brain levels and thus adverse effects. Therefore, this study provides evidence that GABAA-Rs can be a therapeutic target for intervention during intoxications with piperazine derivatives.

236. Pharmacokinetic study of mitragynine in Kratom abuse users

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Objective: To study the pharmacokinetics of mitragynine, the most prevalent alkaloid in Kratom (*Mitragyna speciosa* Korth) in chronic abusers.
Methods: Since Kratom is a drug of abuse and illegal in Thailand, we studied by enrolling 6 healthy male chronic abusers in this study. We adjusted the steady state in each volunteer by giving a known amount of Kratom tea for 7 days before. We admitted and gave the loading dose to all volunteers. The mitragynine blood levels were measured at 17 time points in the 24-hour period, and the total urine level in 24 hours was collected and measured using the liquid chromatography–tandem mass spectrometry (LC–MS/MS) method.
Results: Six volunteers completed the study without adverse reactions. We subgrouped to 3 dose groups as high (23 mg), middle (12.5 mg), and low (6.25 mg) doses. The pharmacokinetic parameters of the 3 groups were as follows: the peak plasma concentration (Cmax) was 28, 45.29, and 116.8 ng/mL; time to reach Cmax (tmax): 45, 70, and 30 minutes; terminal half-life (t1/2) was 12.8, 8.36, and 32.6 hours; and area under the time-concentration curve (AUC) was 93.47, 159.02, and 771.08 mg/mL•h, respectively. Other pharmacokinetic parameters were also reported. The pharmacokinetics were two-compartment model and nonlinear (saturation process).
Conclusion: This was the first pharmacokinetic study in humans. The parameters found in our study were different from those of the animal studies.[1–3] The pharmacokinetic parameters reported are the basic pharmacological information for Kratom which is a new emerging drug of abuse available worldwide and which might be developed medically as a better opioid substitute or pain killer in the future.

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237. Study of lithium pharmacokinetics in the rat according to the three different modalities of human poisoning

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Objectives: Lithium-related neurological toxicity may be severe resulting in seizures, myoclonic encephalopathy, and coma. Three different poisoning presentations exist in humans, including acute poisoning in non-previously treated patients (A), acute-on-chronic poisoning (A/C), and therapeutic overdose (T). The exact reasons why severity and features are different between these three presentations are unknown, although differences in brain lithium distribution have been suggested. Our objective was to study lithium pharmacokinetics in blood and brain in rat models corresponding to each human presentation.
Methods: Development of three models of lithium intoxication in Sprague Dawley rats: A (one intraperitoneal injection of 185 mg/kg Li_2CO_3); A/C (800 or 1600 mg/L Li_2CO_3 in the drinking water followed by one intraperitoneal injection of 185 mg/kg Li_2CO_3 at day 28); T ($K_2Cr_2O_7$-induced acute renal failure on day 1 followed by intraperitoneal injections of 74 mg/kg/day Li_2CO_3 during 5 days); determination of plasma, erythrocyte, cerebrospinal fluid, and brain lithium concentrations using inductively coupled plasma atomic emission spectroscopy (quantification threshold: 0.6 nmol/L); modeling and determination of pharmacokinetics parameters; and comparisons with non-parametric tests.
Results: Lithium followed tricompartmental pharmacokinetics with a shortened plasma half-life in the case of previous chronic exposure (1.73 vs. 3.85h). The peak lithium concentration was measured at 6h in erythrocytes, 2h in cerebrospinal fluid, and 24h in the brain in both A and A/C models; however, the elimination constants k21 (erythrocytes-to-plasma) and k31 (brain-to-plasma) were lower in the A/C model (0.36 versus 0.56 and 2.1 versus 9.2, respectively), suggesting lithium accumulation. The brain distribution was not

homogeneous, with rapid entrance (as soon as 15 minutes), peak at 24h, and delayed elimination (>78h). Lithium accumulation into the brain was more marked in the presence of previous chronic exposure (brain-to-plasma ratio at 54h: 131.27 vs. 6.42; $p < 0.0001$). Similarly, alteration in renal elimination resulted in increased brain distribution (brain-to-plasma ratio: 10.98 vs. 6.88).
Conclusion: Our experimental models suggest that the three different presentations of lithium poisonings in humans differ due to lithium blood pharmacokinetics and brain distribution. However, the hypothesis of an additional variability related to different interactions of lithium with neurological targets in each presentation could not be ruled out.

238. Challenging the limitation of clinical toxicology in the developing world: Where do we go from here?

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Background: To have an impact on clinical toxicology, both the acute clinical syndrome and the underlying socioeconomic and geopolitical factors that drive exposure and response need to be addressed. In the developing world, these factors produce a high baseline burden encompassing a broad spectrum of acute clinical toxicology, predominately from agrochemicals, natural toxins, and pharmaceuticals. In some countries, this is further complicated by weak regulatory frameworks and limitations in response to restrictions in human and infrastructure resources. Coupled with this high baseline, there is an increased risk of acute or chronic surges from toxic outbreaks; examples include methanol, lead, arsenic. The high burden helps expose many important limitations for clinical toxicology that are important globally.
Discussion: Collaborative developed–developing country-funded research projects have provided opportunities for bilateral training and translational research. Once funded, development of local research capacity is limited by lack of local mentors and role models to supervise postgraduates. Wider use of Internet based supervision, site visits, and academic exchange partially addresses this limitation. The paradox is that once the developing world problem of high baseline burden was recognized, it produced a vigorous research response based upon increasing volumes of data collection from both randomized control trials (RCTs) and observational cohorts. This exposed significant limitations in capacity to fully utilize the data. Limitations include limited human resources, not asking a broad enough range of questions and not utilizing more sophisticated statistical analysis. Opening access to our data may allow greater transparency, engagement of other scientists, and regulators. In Sri Lanka, engagement of regulators has led to pesticide bans and a significant reduction in mortality.
Conclusion: Translating evidence into clinical practice is a challenge globally but is particularly heightened in isolated practices especially in health cultures that have not developed a strong evidence-based framework. Both the logistics and local sociological determinants of implementing evidence need to be understood in order to be effective. There may be much greater engagement with broader less controversial primary prevention interventions such as improving adolescent life skills or promoting safer storage practices. To address these areas requires clinical toxicology to engage in broader collaborations with other areas of science and the community.

239. Phosphides and phosphine: Mechanisms for toxicity and range of the problem

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Objective: To investigate epidemiology, probable mechanisms, and recent updates on phosphine toxicity management.
Methods: Google Scholar search engine was applied to review relevant scientific articles published from 2007 to 2013. "aluminum" OR "zinc" phosphide OR phosphine AND "toxicity" OR "poisoning" were used as key words.
Results: Epidemiology: Phosphides are among the most common causes of poisoning with agricultural pesticides with a high mortality rate (30% to 100%). Different phosphide metals including aluminum (AlP), zinc (Zn_3P_2), magnesium (Mg_3P_2), and calcium (Ca_3P_2) are used as pesticides. Intentional ingestion of AlP and Zn_3P_2 has repeatedly been reported from Iran, India, Jordan, Nepal, Egypt, Morocco, and Turkey. In addition to the suicidal reports, inhalational toxicity has been reported in Germany, United Kingdom, France, Denmark, Greece, Australia, and United States.[1–6]

Mechanism of toxicity and toxicokinetics: The exact mechanism of toxicity remains unclear. Upon release of the active phosphine component, which would be faster in the presence of moisture and acidity of the stomach, it is rapidly absorbed through mucosal membranes and reaches the blood stream, distributed to tissues, and is mainly excreted by the kidneys and lungs. Studies show inhibition of different enzymes and protein synthesis including cytochrome-C oxidase, catalase, cholinesterase, and peroxidase leading to cellular damage by high superoxide dismutase, lipid peroxidation, and glutathione reduction. It is known to interact irreversibly with free hemoglobin and hemoglobin in intact erythrocytes to produce a hemichrome, which may explain methemoglobinemia and hemolysis in rare cases.

Clinical manifestations: Failure of cellular respiration may affect each organ; but cardiovascular system, lungs, kidneys, and gastrointestinal tract abnormalities are more common.[3] The signs and symptoms are nonspecific. Early symptoms include nausea, vomiting, retrosternal and epigastric pain, hematemesis, dyspnea, anxiety, agitation, palpitation and foul smell of garlic/calcium-carbide on the breath. Patients remain mentally clear till cerebral hypoxia ensues following shock state. Severe hypotension unresponsive to fluids and vasopressors, severe metabolic acidosis, resistant cardiac arrhythmia, low ejection fraction, comprised of ST and T-wave changes, pulmonary edema and cyanosis are usually bad prognostic factors. Other rare effects include adrenal insufficiency, hepatitis, acute tubular necrosis, disseminated intravascular coagulation, hemolysis, methemoglobinemia, respiratory alkalosis, pleural effusion and ascites, rhabdomyolysis, and pancreatitis.[1–6]
Diagnosis: Diagnosis is based on the patient's history and positive results (blackening) of the silver-nitrate test strips when moistened with the patient's exhalation of PH_3 or by biochemical analysis of blood or gastric aspirate for phosphine.[3] In some places, tablets of AlP are also referred to as "rice tablets," and if there is a history of ingestion, it should be differentiated from other types of rice tablet made up of herbal products.[6] Co-oximetry may play a role in diagnosing/predicting life-threatening AlP poisoning. Oxyhemoglobin may be affected by phosphine and produce a dyshemoglobin that interferes with CO light absorption.[7]

Management: There is no known antidote for metal phosphide poisoning, and therefore, management remains primarily supportive focusing on airway patency and protection, supplementary oxygen, intravenous access (preferably central venous), and starting fluids and vasopressor therapy as indicated. Early identification of impending organ failure and appropriate supportive care is important till the toxin is excreted. Close monitoring of vital signs should include electrocardiogram (ECG), chest X-ray, blood glucose, arterial blood gas, electrolytes including magnesium and calcium, and liver and renal function tests. Repeated or continuous ECG and echocardiography can reveal cardiac dysfunction early. Occupational or accidental inhalational exposures need rapid evacuation and administration of fresh air/oxygen. Early arrival, vomiting, resuscitation, prompt diagnosis, intensive monitoring, and supportive therapy may result in good outcome. Due to rapid phosphine absorption, there is doubt on the effectiveness of activated charcoal, paraffin oils, coconut oil, and even gastric washing by sodium bicarbonate or potassium permanganate although some animal studies show that it may reduce the toxicity of metal phosphides.[1–6] Gastric-ventilation may be applied for a limited time when phosphine is being released in the gut to prevent its mucosal absorption, but further clinical trials are required to confirm its efficacy.[8] For refractory hypotension, norepinephrine or phenylephrine could be used. Anti-arrhythmic agents, DC cardioversion, and temporary pacemaker should be available for severe cases. Antioxidants including N-acetylcysteine, vitamins E and C, glutathione, melatonin, and beta carotene have been tried but need further trials before their routine use. Magnesium supplementation terminates atrial fibrillation, SVT and VT in some studies, but there are other studies against their efficacy. While acetylcholinesterase activity may be inhibited by phosphides, atropine and pralidoxime may play a therapeutic role; however, evidence is not enough.

Oral administration of trimetazidine, an anti-ischemic drug that works through decreasing the production of oxygen-derived free radicals and stopping ventricular ectopic beats and bigeminy, has been suggested. Temporary pacemaker and intra-aortic balloon pump may successfully be applied when pharmaceuticals could not prevent/treat cardiovascular complications.[1–6] Hyperinsulinemia-euglycemia and hyperventilation-oxygenation therapy may improve cell viability through restoring calcium fluxes and improving myocardial contractility.[9]

Conclusion: Exposure to phosphine gas released from metal phosphides increases risks of major morbidity and mortality. Clinician knowledge should be increased with an emphasis on prevention, diagnosis, and management. Fast change from normal to life-threatening symptoms, difficult therapeutic modalities to overcome this intoxication and limited evidence on the efficacy of therapeutic interventions pose challenges to the clinicians.

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240. Ayurvedic drugs: Its a jungle out there

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Background: Ayurveda means "the complete knowledge for long life"; in Sanskrit, the words āyus, means "longevity", and veda means "related to knowledge" or "science". Western medicine has classified Ayurveda as a system of complementary and alternative medicine (CAM) that is used to complement, rather than to replace, the treatment regimen and relationship that exists between a patient and their existing physician. This presentation aims to highlight the causes of toxicity due to ayurvedic medicines.

Discussion: Ayurvedic medication is aimed at prevention, promoting healthy habits and treating the illness. Ayurvedic medicines are also classified into three groups: (1) kastha ausadhis (herbal preparations); (2) rasa ausadhis (metallic preparations [bhasmas, sindoora]);and (3) jangama ausadhis (animal preparation – prepared from animal products). Being herbal, the ayurvedic medicines are considered harmless but a few side effects have been reported but they are rare. "Herbal" does not mean "harmless" (free of side effects) or even "non-poisonous". Ayurvedic medicines have not been subjected to the same rigorous testing as conventional medicine. There may be potential side effects. According to a study conducted in the United States, ayurvedic medicines sold over-the-counter were high in heavy metal content. The source of toxicity could be the herb itself, there could be changes in the way the raw material is processed and the final product could have interactions with other drugs. The reasons why these medications may be toxic could be attributed to the environment and conditions i.e., the way the medicinal plants are grown or collected or the conditions under which they are dried and processed or stored and transported. The manufacturing processes could be faulty with the addition of potentiating herbs or synthetic drugs and the mixing with heavy metals. Finally, the loose regulations safeguarding the quality of the herbal agents could be responsible for toxicities.

Conclusion: All herbal/ayurvedic medicines have the potential to be toxic. Stricter quality control measures would go a long way in preventing harmful effects of ayurvedic drugs.

241. Setting up poison information services in developing countries–needs and accomplishments: The Poison Control Centre of Senegal

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Introduction: With both domestic and professional cases of poisoning particularly due to chemicals in the developing countries, the Intergovernmental Committee on Chemical Security, at the 3rd Forum of Salvador da Bahia (Brazil, March 22, 2000), suggested the creation of appropriate structures to improve public health concerns.
Discussion: In accordance with this commitment, Senegal decided to create a poison control center (PCC) in 2004 in the offices of the Health Ministry. Senegal PCC consists of several functional units. Its mission is to ensure the prevention of poisoning caused by xenobiotics, including pharmaceutical products, pesticides, household products, industrial products, envenomations, and plants, improving their management support and monitoring their effects on health. The center has an operating budget allocated by the Senegalese government that has allowed it to carry out certain activities, only since August 2009. Toxicological information and telephone response represent the main activities and are performed 24h/24 using a phone number for emergency calls. During the first 4 years, 264 calls were recorded: 30 cases (2009), 68 cases (2010), 84 cases (2011), and 82 cases (2012). Other activities within the service allow our PCC to function, as well as have representation in other health structures. Our PCC conducts pharmacovigilance by investigating the causal relationship of the suspected pharmaceuticals. This was performed in 663 cases since 2009. The prospects of our PCC are numerous in order to improve its efficiency as well as the management of poisoning and envenomations in the country. However, these objectives are difficult to achieve due to the lack of resources: human, logistical, and financial.
Conclusion: In conclusion, a PCC is essential in an emerging country and requires the support of partners from the developed world to carry out its activities in order to achieve the millennium development goals (MDGs).

242. Feasibility study for a sub-regional poisons centre in the Eastern Africa sub-region

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Background: The African continent is burdened by similar, or more severe, toxicological issues as other continents, yet only a few poisons centres exist to assist in the management of poisoning. In the Eastern Africa (EA) sub-region, there are poisons centres in 2 countries: Kenya and Zimbabwe. The Strategic Approach to International Chemicals Management (SAICM) Quick Start Programme funded a project to find a means for improving provision of poisons centre services in Africa. The specific objectives were to document the incidence of poisoning in the East African sub-region; establish the existing provision of poisons centre services in the sub-region; identify available models of poisons centre service provision and the requirements for their establishment; and present options for ways of improving the availability of poisons centre services in the sub-region.
Methods: A literature review and questionnaire survey as well as national and international multi-stakeholder consultations were undertaken to gather available data on poisoning in the region. Sixteen countries were studied, with in depth analysis of four.
Results: Few data were found on poisoning in the sub-region; however, poisoning with pesticides, kerosene, traditional medicines, and natural toxins were reported, in some cases with relatively high case fatality rates. Most countries suffered a shortage of healthcare personnel, and had largely rural populations. Telecommunication infrastructure is developing quickly in many countries. The need for and enthusiasm to expand current poison centre capacity was demonstrated. Countries preferred to have national centres rather than a sub-regional centre, but strongly supported the concept of a hub function to link the centres. The Network of African Poisons Centres and Applied Toxicologists was identified as a key player. Other project outputs included proposals for four new national centres, a toolkit for poisons centre development and a document on sustainable funding.
Conclusion: National poisons centres supported by a hub that can provide coordination, training and advocacy with governments and regional economic communities was the preferred approach. Poisons centres are needed to address the current and future burden presented by poisoning, as well as to meet national needs to comply with international conventions and the International Health Regulations.

243. Methanol and formate elimination half-life during treatment for methanol poisoning: Intermittent hemodialysis versus continuous hemodialysis/hemodiafiltration

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Objective: To study the methanol and formate elimination half-lives on intermittent hemodialysis (IHD) and continuous veno-venous hemodialysis/hemodiafiltration (CVVHD/HDF) and the impact of dialysate/blood flow rates on elimination.

Methods: Data were obtained from a prospective study on 24 patients: IHD was used in 11 and CVVHD/HDF in 13 patients. Serum methanol and formate concentrations were measured by gas chromatography and an enzymatic method, respectively. Half-lives were compared by unpaired Student's t-test and by multivariate regression for normally distributed data.
Results: The groups were comparable by all parameters, with the CVVHD/HDFgroup being slightly more acidotic (mean pH, 6.9 ± 0.1 vs. 7.1 ± 0.1). The mean elimination half-life of methanol was 3.7 ± 1.4 and of formate was 1.6 ± 0.4 hours on IHD, versus 8.1 ± 1.2 and 3.6 ± 1.0 hours on CVVHD/HDF ($p < 0.001$). The half-lives were shorter when the blood flow rates were higher (T½ methanol = 13.931-0.042*x, $R^2 = 0.524$; T½ formate = 6.505-0.020*x, $R^2 = 0.439$; $p < 0.001$). In CVVHD/HDF, the elimination half-lives were shorter when the dialyzate flow rate was higher (T½ methanol = 10.909-0.0011*x, $R^2 = 0.121$, $p = 0.015$), and the dialyzer membrane was larger (T½ methanol = 17.372–5.488*x, $R^2 = 0.442$, $p = 0.013$; T½ formate = 9.867-3.713*x, $R^2 = 0.324$, $p = 0.042$). In IHD correlation was found between the dialyzer membrane surface and the elimination half-life of methanol (T½ methanol = 48.886-28.857*x, $R^2 = 0.503$, $p = 0.015$). No correlation was present between the elimination half-lives and the pre-dialysis serum concentrations of methanol, formate, ethanol, bicarbonates, and lactate (all $p > 0.05$). Correlation was present between the half-life of formate and arterial blood pH, and the longer half-life of formate was present in more acidotic patients ($p = 0.038$). The patients with visual/central nervous system sequelae had a longer elimination half-life of formate ($R^2 = 0.309$, $p = 0.005$).
Conclusion: The 54% reduction in methanol and 56% in formate elimination half-life during IHD results from the higher blood and dialysate flow rates. Increased blood and dialysate flow on the CVVHD/HDF also increased the elimination. Our study supports the superiority of IHD over CVVHD/HDF in terms of methanol and formate elimination. We recommend optimizing dialysis by increasing the blood and dialysate flow as much as possible given the limitations of the apparatus and the patient conditions. If the methanol concentration or the osmolal gap cannot be measured, we recommend at least 8 hours (IHD) or 18 hours (CVVHD/HDF) of dialysis before discontinuation.

244. α-Amanitin poisoning: Outcome in 242 patients treated with the Pavia mushroom protocol (N-acetylcysteine, forced diuresis and multiple-dose activated charcoal)

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Objective: To evaluate the clinical course and outcome of patients with α-amanitin poisoning confirmed through urinary detection of the toxin and treated with N-acetylcysteine (NAC), forced diuresis (FD), and multiple-dose activated charcoal (MDAC).
Methods: We retrospectively (January 2002–December 2012) reviewed all patients (i) admitted to emergency departments all over Italy and referred to Pavia Poison Control Centre, with (ii) gastrointestinal symptoms after at least 6 hours from uncontrolled mushroom consumption, and with (iii) laboratory confirmation of urinary α-amanitin toxic levels (≥ 5 ng/mL). Specific treatment included NAC (intravenous 150 mg/kg followed by 300 mg/kg/day until 48 hours after mushroom ingestion in patients without hepatitis and as long as ALT < 200 UI/L in patients with hepatic damage), FD until negative urinary α-amanitin levels, and MDAC (2-5 g/h) until 96 hours. Hepatic damage was defined using ALT acme during hospitalization: absent (ALT < 49 UI/L), mild (ALT 50–199 UI/L), moderate (ALT 200–2000 UI/L), and severe (ALT > 2000 UI/L). Outcome was evaluated as absence of hepatitis, fully recovered, organ transplantation, and death.
Results: Two hundred and forty-two patients (mean age, 53 ± 19 years) were included. At first medical evaluation 167/242 (69%), patients presented normal hepatic function (group 0), whereas 31/242 (12.81%), 37/242 (15.29%), and 7/242 (2.89%) presented mild (group 1), moderate (group 2), and severe (group 3) hepatic damage, respectively. In group 0, 83/167 patients (49.7%) did not develop hepatitis. Among the 75 patients that presented hepatic damage at admission (groups 1, 2 and 3), 32 (42.66%) did not worsen after the treatment was started, while for 43 (57.33%) their hepatic damage worsened. Overall for 242 patients the urinary α-amanitin mean value was 39.21 ± 30.67 ng/mL. NAC treatment was started on average 28.08 ± 14.41 hours after mushroom ingestion and was performed until normalization of hepatic function. No adverse reactions were registered. The overall unfavorable outcome (considering both death and liver transplantation) was 4.1% (10/242); only 5 fatal cases (2%) were registered.
Conclusion: The observed mortality rate is lower than in other published case series that, moreover, did not consider the urinary α-amanitin level among the inclusion criteria.[1,2]

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245. Arteriovenous extracorporeal life support in drug-induced cardiogenic shock: A10-year experience

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Objectives: Arteriovenous extracorporeal life support (ECLSav) is now considered in acute poisonings resulting in refractory cardiogenic shock (RCS) and even refractory cardiac arrest (RCA). We would like to report a 10-year experience using ECLSav in acutely poisoned patients.
Case series: A cohort from 2002 to 2012 of patients admitted at our medical and toxicological intensive care unit for drug-induced RCS and/or RCA. Indication of ECLSav was set owing to the onset

of cardiogenic shock refractory to betamimetic agents or RCA. Arterial and venous cannulae were set using a surgical procedure already reported. ECLSav was performed using the Rotaflow® Jostra-Maquette device with oxygenator Quadrox PLS. Results are expressed as median (extremes) or percentage. Primary endpoint was final outcome.

Results: Three hundred and thirty-two ECLSav were performed over 10 years. RCS and/or RCA resulted from drug poisonings in 112 cases (34%). The leading causes were chloroquine (19), propranolol (9), acebutolol (9), verapamil (7), flecainide (7), venlafaxine (5), colchicine (4), meprobamate (3), cyamemazine (3), cocaine (3), clomipramine (3), and cibenzoline (3). RCA during the setting of ECLSav was recorded in 71 cases occurring out-of-hospital (OH) in 45 (63%) cases and in 26 (37%) cases in-hospital (IH). The median delay between onset of RCA and ECLS was 136 min (59–381). Global survival rate of OH and IH RAC were 11% (5/45) and 14% (3/26), respectively. RCS with or without transient CA was the condition of ECLSav in 41 cases occurring OH in 7% (3/41) cases and IH in 38/41 (93%) cases. Survival rates of EH and IH were 100% (3/3) and 47% (18/38), respectively. By toxicant, the survival rates were chloroquine 10% (2/19), propranolol 55% (5/9), acebutolol 55% (5/9), verapamil 14% (1/7), flecainide 28% (2/7), venlafaxine 0% (0/5), meprobamate 0% (0/3), cyamemazine 0% (0/3), cocaine 0% (0/3), clomipramine 0% (0/3), cibenzoline 66% (2/3), and colchicine 0% (0/4).

Conclusion: ECLSav was associated with an improvement in prognosis in beta-blockers and membrane-stabilizing agents except for chloroquine. The improvement in verapamil poisonings is questionable. The poor prognosis in psychotropic drugs inducing RCA/RCS suggests hemodynamic failure resulted from hypoxic rather than from cardiotoxic effects.

246. The pharmacology of novel psychoactive substances

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Objective: The aim of the study was to characterize the *in vitro* pharmacology of a series of amphetamine-type novel psychoactive substances (NPS) including cathinones (bath salts), piperazines, and aminoindanes.

Methods: We assessed 3H-monoamine uptake and reverse transport in HEK 293 cells expressing the human serotonin-, norepinephrine-, or dopamine-reuptake transporters (SERT, NET, or DAT, respectively). Binding affinities at monoaminergic receptors were assessed using displacement of radioactive ligands.

Results: There was considerable heterogeneity in the mechanism of action of NPS tested in this study (17 cathinones, 3 aminoindanes, 3 piperazines, and 2 methylphenidate-like drugs). Mephedrone and methylone were cathinones which were equipotent SERT/NET/DAT inhibitors similar to cocaine but also produced serotonin release via SERT similar to MDMA (Ecstasy). Cathinone, methcathinone, and flephedrone were methamphetamine-like cathinones which were preferential DAT/NET inhibitors and dopamine releasers. Pyrovalerone-type cathinones such as pyrovalerone and MDPV were selective and very potent DAT/NET inhibitors similar to D2PM and 2-DPMP which are structurally similar to methylphenidate. Furthermore, the ring-substituted amphetamines PMA, PMMA, and 4-MTA, the aminoindanes 5-IAI and MDAI, and the phenylpiperazines TFMPP and m-CPP preferentially acted at SERT and NET similar to MDMA, while the aminoindane 2-AI and benzylpiperazine selectively blocked and reversed NET and DAT function. The NPS studied here did not exhibit high affinity to brain receptors besides the monoamine transporters, suggesting that they mostly act as indirect agonists at the monoaminergic systems similar to the classic amphetamines. However, the serotonergic vs. dopaminergic properties varied dramatically between these NPS.

Conclusion: The mode of action of novel cathinones, aminoindanes, and piperazines is overall similar to that of the classic amphetamines. However, within the groups, there are considerable pharmacological differences with regard to the selectivity of the drugs for the SERT or DAT which are likely to influence the clinical toxicity and abuse liability of these novel compounds.

247. Novel and emerging recreational drug detection: A signals intelligence approach

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Objective: US data source limitations render them ineffective when applied to novel psychoactive compounds (NPACs). Delays in data compilation, manuscript preparation, review, and publication compromise even the best investigations. Sampling deficiencies may occur in geographic distribution or demographic groups. Sources are incomplete due to methodology that does not capture novel drug data or conflates it with other drugs. We evaluated emerging NPACs, applying signals intelligence by examining spontaneous self-reported drug experiences, Internet searches, and web-based encyclopedia content.

Methods: The Erowid database of user experiences (http://www.erowid.org/experiences/exp.cgi), Google Trends (http://www.google.com/trends/), and Wikipedia (http://www.wikipedia.org/) were examined retrospectively from 2004 through 2012. Erowid, Google Trends, and Wikipedia initial NPAC report, search, and posting dates were compared. Time differences (recorded in months) for Erowid versus Google Trends, Wikipedia versus Google Trends, and Erowid versus Wikipedia were calculated using simple statistics.

Results: Erowid user drug experiences totaled 16,055. A review of account usernames showed that 86.8% of Erowid users posted a single Erowid experience report. The Erowid database yielded 67 NPACs for the study period. Google Trends recognized 42 of these. Erowid experiences appeared a median of 0.5 months after compared to Google Trends (interquartile range (IQR), 13.3 months prior to 12 months after). Wikipedia content predated Google Trends by a median of 17 months (IQR, 44 months to 3.0 months prior). Initial Wikipedia posts predated Erowid by a median 7.5 months (IQR, 31 to 1 month prior). Twenty-one compounds (31.3% of total) were mentioned only in Erowid and Wikipedia. Erowid reports appeared a median 71 months prior to the conclusion of the study period (IQR, 103 to 22 months prior). NPAC Wikipedia articles similarly were posted a median

71 months prior to the conclusion of the study period (IQR, 86 to 63 months prior). Four compounds (2C-D-NBOMe, 2C-G-NBOMe, 4-AcO-DALT, and 4-AcO-EIPT) were discovered solely in Erowid experiences, an average of 26.8 months prior to the conclusion of the study period.
Conclusion: Diverse, open-source Internet-based self-reported experiences, search strategies, and content can inform the analysis of NPAC introduction and diffusion. If automated, this methodology could support ongoing surveillance epidemiology to provide leading edge indicators for emergent drug phenomena.

248. Novel synthetic cannabinoid outbreak causing severe illness

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Objective: Previous synthetic cannabinoid (SC) reports suggested a benign clinical syndrome.[1] Recently, an SC product known as "spice" or "black mamba" resulted in increased severe presentations to emergency departments (EDs) in Colorado, USA. Coordinated efforts between medical toxicologists, public health, the Centers for Disease Control (CDC), and law enforcement identified the cause and decreased exposures. Spectrophotometry identified ADB-PINACA, a novel SC, in multiple seized products from exposed patients. Our objective is to describe the illness spectrum and patient management during this outbreak.
Methods: This retrospective cohort study includes all patients with SC exposures presenting to two urban academic EDs from 24 August to 13 September 2013. Subjects were identified through poison center calls, mandatory public health ED reporting, and ED discharge diagnoses. Medical records were abstracted for demographics, clinical variables, and treatments.
Results: Seventy-six patients with SC exposure presented during the study period. Median age was 28 years (interquartile range [IQR]: 23–35); 72.3% were male. Presenting symptoms included altered mental status (67.6%), agitation (42.1%), and seizures (14.4%). Other findings included elevated creatinine (34.2%), hyperthermia (11.8%), and respiratory failure requiring intubation (9.2%). While patients were initially tachycardic (median, 100 bpm [IQR: 82,115]), relative bradycardia later developed (median 63 bpm [IQR: 56,73]); 10% had a heart rate of ≤ 50 bpm. For sedation, 42.1% received benzodiazepines, 14.4% antipsychotics, and 2.6% ketamine. Most patients (89.5%) were managed in the ED; however, 9.2% were admitted to intensive care units.
Conclusion: In contrast to first-generation SC exposures[1], more recent SC cases were associated with seizures[2] and cardiotoxicity[3], possibly due to increased SC potency. ADB-PINACA exposure in this outbreak was associated with neurotoxicity and cardiotoxicity.

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249. Acute effects of methylphenidate in healthy subjects alone or in combination with MDMA

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Objective: Methylphenidate is misused as a cognitive enhancer and recreationally by healthy subjects. 3,4-Methylenedioxymethamphetamine (MDMA, "ecstasy") is a popular recreational substance. The aim of this study was to assess the autonomic, adverse, and subjective dose-dependent effects of single doses of methylphenidate in healthy subjects as well as its pharmacodynamic interaction with MDMA.
Methods: First, we assessed the acute effects of methylphenidate (40 mg) compared with placebo in 30 healthy subjects. Second, we assessed acute effects of a high dose of methylphenidate (60 mg) compared with placebo, MDMA (125 mg), or with the combination between methylphenidate (60 mg) and MDMA (125 mg) in another 16 healthy subjects. Outcome measures were blood pressure, heart rate, core body temperature, adverse effects, and subjective drug effects assessed up to 24 hours.
Results: Both doses of methylphenidate significantly increased blood pressure and heart rate compared with placebo (all $p < 0.001$). The high dose of methylphenidate tended to increase the blood pressure more than the low dose. The high dose of methylphenidate also significantly increased body temperature compared with placebo ($p < 0.001$). Both doses of methylphenidate enhanced good subjective drug effects, stimulation, and alertness (all $p < 0.05$). Subjective effects were dose dependent. Acute adverse effects up to 5h were increased by both doses, and the high dose of methylphenidate also significantly increased subacute adverse effects up to 24h after drug administration compared with placebo. Adverse effects were dose dependent. MDMA produced more positive subjective drug effects but less activity and concentration compared with methylphenidate. When methylphenidate and MDMA were administered together, the combination produced similar subjective effects compared with MDMA alone but the cardiovascular and adverse effects were significantly higher compared with those of either drug alone (all $p < 0.01$).
Conclusion: Acute administration of methylphenidate to healthy subjects produces significant cardiovascular stimulation and adverse effects in a dose-dependent manner. Co-administration of MDMA and methylphenidate did not produce more psychotropic effects than MDMA alone but enhances cardiovascular and adverse effects of either drug alone.

250. Enhanced elimination methods in treatment of acute methanol poisonings: Continuous hemodialysis/hemodiafiltration versus intermittent hemodialysis

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Objective: During an outbreak of methanol poisonings in the Czech Republic in 2012, we studied the comparative effect of intermittent hemodialysis (IHD) and continuous veno-venous hemodialysis/hemodiafiltration (CVVHD/HDF) on the treatment outcome in methanol poisonings.

Methods: Data were obtained from a retrospective case series study on 75 patients: IHD was used in 30 and CVVHD/HDF in 45 patients. The patients were treated with alkalinization, antidotes (ethanol or fomepizole), folate administration, and hemodialysis. The laboratory data on admission, clinical features, treatment measures, and outcomes in the groups were compared using unpaired Student's t-test. The exploratory factor analysis on Spearman and Pearson correlations between the treatment outcomes (survived without sequelae, survived with sequelae, died) and the monitored input variables were used.

Results: The groups of patients were comparable by age, time to diagnosis, laboratory data, clinical symptoms on admission, and treatment measures. The group on CVVHD/HDF was more acidotic (mean pH, 6.99 ± 0.08 vs. 7.16 ± 0.09, $p = 0.006$). A significant correlation was present between the treatment outcome and severity of metabolic acidosis expressed by pH, base deficit (BD), anion gap, bicarbonate, and lactate (all $p < 0.01$). A significant correlation was present between the mode of hemodialysis and the treatment outcome ($r_s = 0.251$; $p < 0.01$). No significant correlation was found with specific antidote (fomepizole) administration ($r_s = 0.124$; $p > 0.05$), folate substitution ($r_s = 0.149$; $p > 0.05$), and the treatment outcome. The difference in the ratio died/survivors between IHD and CVVHD/HDF was not statistically significant ($p = 0.412$). The rate of survival in the patients with pH < 7.0, BD > 25, poisoning severity score (PSS) 3, APACHE > 20, or Glasgow Coma Score (GCS)< 6 did not differ significantly between the groups (all $p > 0.05$). But more patients without visual and central nervous system (CNS) sequelae of acute methanol intoxication were in the group of patients treated with IHD (67% vs. 42%, $p = 0.038$).

Conclusion: The number of treatment outcomes without visual and CNS sequelae was higher on IHD, which can be attributed to the higher rate of formate elimination, and probably more rapid correction of metabolic acidosis compared to CVVHD/HDF. But the survival rate, especially in the late-presenting patients with severe metabolic acidosis and coma on admission, was not significantly influenced by the mode of hemodialysis.

251. Electrocardiographic predictors of adverse cardiovascular events in acute drug overdose: A validation study

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Objectives: To validate our prior findings[1] that features of the initial electrocardiogram (ECG) are associated with adverse cardiovascular events (ACVE) among emergency department (ED) patients with acute drug overdose (ADO).

Methods: We performed a prospective validation cohort study to evaluate adult ED patients with ADO at two urban university hospitals over 5 years in whom on ED admission ECG was performed. Excluded were patients with alternate diagnoses, anaphylaxis, chronic drug toxicity, and missing outcome data. ACVE was defined as any of the following: shock (vasopressor requirement), myocardial injury (MI, elevated troponin), ventricular dysrhythmia, or cardiac arrest (pulseless). Blinded cardiologists interpreted ECGs for rhythm, intervals, QT dispersion (QTD), ischemia (T wave inversion, ST depression), and infarction (ST elevation, Q waves). Diagnostic test characteristics of our previously derived ECG rule (ectopy, non-sinus rhythm, and QTc),[1] as well as univariate statistics, odds ratios (OR), and 95% confidence intervals (CI), were calculated.

Results: Of 589 ADO patients who met inclusion criteria (48% male; mean age, 42 years), there were 95 ACVEs (39 shock, 64 MI, 26 dysrhythmia, and 16 cardiac arrest). The most common drug exposures were benzodiazepines, opioids, and paracetamol. Diagnostic test characteristics of the ECG rule as well as high-risk ECG features are illustrated in Table 1.

Conclusion: This study validates previously derived high-risk features of the admission ECG (ectopy, QTc, rhythm, ischemia, and infarction) to risk stratify for ACVE in ED ADO patients. Test characteristics of the ECG alone were not sufficient to exclude likelihood of ACVE.

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252. Respiratory failure from acute drug overdose: Incidence, complications, and risk factors

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Background: Drug overdose is the leading cause of injury-related fatality in the United States and likely elsewhere, and respiratory

Table 1. ECG predictors of ACVE in ED ADO patients.

ECG Variables:	Bivariate p value:	OR (CI) for ACVE:
	ECG Factors:	
Non-sinus rhythm	<0.001	8.9 (3.9–19.9)
Ectopy	<0.001	5.3 (2.2–12.3)
QT Prolonged (≥ 470 ms)	<0.001	2.7 (1.5–4.6)
QTc Severe (≥ 500 ms)	<0.001	11.2 (4.6–27)
QTD (≥ 50 ms)	<0.01	2.2 (1.3–3.7)
Ischemia	<0.001	5.0 (2.9–8.5)
Infarction	<0.01	2.3 (1.2–4.2)
	ECG Rule	
	(1) Ectopy; (2) QT prolonged; (3) non-sinus rhythm; and (4) ischemia/infarction	

Sensitivity (CI)	Specificity (CI)	NPV (CI)	OR (CI) For ACVE:
68.4% (58–78)	68.6% (64–73)	91.9% (87–94)	4.7 (2.9–7.6)

failure (RF) remains a major source of morbidity and mortality. However, neither the incidence nor risk factors for RF in overdose patients are currently known.

Methods: Secondary data analysis was performed from a prospective cohort of adult emergency department (ED) patients with acute drug overdose at two urban tertiary-care hospitals over a 5-year period. Excluded were patients with alternate diagnoses, anaphylaxis, chronic drug toxicity, and missing outcome data. ED clinical data included demographics, congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD defined as one of the following: asthma, chronic bronchitis, or emphysema), drug information/screens, blood gas analysis, indications for endotracheal intubation (ETI), details of ETI (location, drugs, complications), and in-hospital mortality. The study outcome was RF defined requirement for mechanical ventilation. Assuming 4% incidence of RF, we calculated the need to analyze 2500 patients to show 150% increased risk from common predictors with an 80% power. Univariate analysis (chi-squared, t-test), 95% confidence intervals (CI), and multivariable logistic regression were performed with SPSS software.

Results: We analyzed 2,497 patients (mean age, 45 years; 54% male) of whom 87 (3.5%) had RF requiring ETI. Prehospital ETI was slightly associated with increased mortality (odds ratio (OR) 2.0, $p = 0.28$) compared with ED and inpatient ETI. Complications of ETI included desaturation (3.4%) and bradycardia (1%). Risk factors for RF included older age ($p = 0.06$) and history of COPD ($p < 0.001$); gender, type of drug exposures, and CHF had no association. After controlling for confounders, COPD was associated with a significantly increased risk of RF (adjusted OR, 6.6; CI, 3.5–12.3). Patients with COPD had higher PCO_2 (54.6 mmHg vs. 47.9, $p < 0.01$) and lower pH (7.31 vs. 7.36, $p < 0.01$) than patients without COPD.

Conclusion: RF infrequently occurred in ED patients with acute drug overdose. Risk factors for RF included age and COPD history, and ETI was frequently uncomplicated. Early ED blood gas analysis may be helpful to identify overdose patients at risk of RF. These results suggest a role for end tidal CO_2 which should be addressed in future studies.

253. Metformin removal by extracorporeal elimination techniques in cases of overdose: A literature review

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Objective: We reviewed the literature to evaluate the role of extracorporeal elimination techniques (EET) in removing metformin in both poisoning and therapeutic use.

Methods: Cases of metformin overdose (articles in English), in which an EET was performed and the amount of removed metformin was measured or calculated, were reviewed using MEDLINE database (from 1988 to October 2013).

Results: We identified 52 articles; nevertheless, the amount of metformin removed was reported in only four studies. Nguyen[1] calculated a high metformin percentage removal (60%) simply using its serum concentration pre- and post-haemodialysis; but this calculation is questionable. Barrueto[2], in a poisoning by ingestion of 20 g, calculated the amount of metformin removed (3465 mg) by multiplying serum concentration, clearance, and time of continuous veno-venous haemodialysis. Zoppellari[3] measured the amount of metformin removed by haemodiafiltration in the ultrafiltrate, and documented a small removal (1068 mg), in a case due to therapeutic use (3000 mg/day), but in a setting of renal failure. Similar results were found by Lalau[4] in three patients on metformin therapy (daily dosages of 3400, 2550, and 1700 mg): the amount removed by dialysis was 1105, 694 and 688 mg, respectively.

Conclusion: Clinical improvement was seen using EET, but only a few studies investigated the amount removed: the benefit is to restore an acceptable acid–base status and to remove the drug. Nevertheless, owing to the small amount of removal of the drug itself, the real benefit of EET was particularly due to the correction of the drug's resultant severe lactic acidosis.

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254. Intravenous lipid emulsion used in the therapy of a patient with prolonged cardiac pauses following a single pill ingestion of propafenone

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Objective: Propafenone is a class IC antiarrhythmic that shares properties with beta-blockers and L-type calcium-channels blockers. "Pill in the pocket" treatment with propafenone is often recommended as a potential therapy for symptomatic paroxysmal rapid atrial fibrillation. We report a patient who developed asystole followed by episodes of prolonged cardiac pauses after her first dose of 150 mg of propafenone. The patient had symptomatic improvement after administration of intravenous lipid emulsion therapy.
Case report: A 78-year-old woman with a past medical history of symptomatic rapid atrial fibrillation was started on 150 mg propafenone orally. The patient took her first dose at approximately 9:30 am. At 1:45 pm, she felt nauseous, light-headed, and had a syncopal episode. Upon paramedic arrival, the patient was awake; however, as she was being moved onto their stretcher, she lost consciousness and was found to be in asystole. Chest compressions were performed and she received atropine 0.5 mg. Thirty seconds later, she had return of spontaneous circulation with no recollection of the event. Her vital signs in the emergency department were blood pressure, 130/80 mmHg; heart rate, 37/min; respiratory rate, 14/min; temperature, and afebrile. The patient had frequent 6- to 10-second pauses on the monitor; during these periods, she complained of nausea and feeling unwell. She was treated with calcium 1 gram gluconate intravenously (IV), 0.5 mg atropine twice, and 3 mg glucagon IV once with minimal improvement. Sodium bicarbonate was not given, as the patient's QRS duration was 76 msec. Due to the failure to improve with conventional therapy, she received a 90 mL bolus of 20% intravenous lipid emulsion with symptomatic improvement and a decrease in the incidence and duration of the sinus pauses. Her heart rate improved to 70 beats/minute. During the hospital admission, she received an ablation as a treatment for her atrial fibrillation and was discharged home 3 days following initial presentation.
Conclusion: We report a case of a patient who developed pronounced toxicity in the setting of a single pill ingestion of propafenone. Propafenone has a Log P of 4.63 and a Log D of 2.39, which allows for the biological plausibility of intravenous lipid emulsion success in the setting of toxicity.

255. Body packing and body stuffing: Review of a case study and proposal for a decision algorithm

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Objective: Body packing and stuffing represent an emergent problem worldwide with associated risks including acute intoxication and bowel obstruction. In recent years, mortality and morbidity have progressively diminished due to appropriate clinical management and a better packaging of illicit substances, thus leading to a more conservative approach.
Methods: From January 2000 to August 2013, we observed 82 patients with diagnosis of suspected packing (n 48) or stuffing (n 34). Seventy-six patients agreed to radiological confirmation (X-ray 15, computed tomography (CT) 23, X-ray + CT 39). Once admitted, the patients underwent vital signs monitoring, oral administration of polyethylene glycol (PEG), and qualitative and quantitative check of retrieved packs. Moreover, 73 patients were radiologically checked to confirm pack elimination.
Results: Twenty-two patients (9 packers and 13 stuffers) showed signs/symptoms of mild to moderate intoxication. In 3 cases, surgical pack removal was necessary (1 for severe cocaine intoxication, 1 for gastric retention, and 1 for bowel obstruction), while 1 patient underwent endoscopic removal for prolonged pack retention at gastric level. One patient presenting heroin overdose was misleadingly sent to the surgeon as CT scan falsely attributed positive images to heroin-containing wrappings. The average hospital stay was similar for packers and stuffers (25 hours; range, 1–164h).
Conclusion: Body drug concealment is still a behavior that can pose life-threatening risks, requiring a multi-disciplinary diagnostic and therapeutic approach. So far, no guidelines or standardized procedures exist for the management of such patients. However, our results confirm the appropriateness of a conservative approach in most cases, supplemented with a surgical procedure only in severely ill patients (leaking packages and bowel obstruction). The CT scan proved to be more sensitive and specific vs. X-ray imaging in defining both pack consumption and elimination monitoring. Considering our experience and the literature,[1] we propose to adopt in these patients an algorithm in order to optimize management, hospital stay duration, and complete pack elimination.

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256. Lisdexamfetamine ingestion resulting in hypertensive emergency treated with phentolamine

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Objective: Lisdexamfetamine is a prodrug of dexamfetamine used in the treatment of attention deficit hyperactivity disorder (ADHD). Very few cases describe toxicity in overdose. We describe a case of overdose with delayed stimulant effects including hypertensive emergency that was treated successfully with phentolamine.
Case report: A 17-year-old female with prior intentional self-poisoning was brought to the emergency department 30 minutes after ingesting fifty 40-mg tablets of lisdexamfetamine. Initial vitals were: temperature 37 C, heart rate (HR) 76 beats-minute, and blood pressure (BP) 108/65 mmHg. No diaphoresis, tremor, mydriasis, or other sympathomimetic effects were seen. She remained essentially asymptomatic until 7 hours post-ingestion when she developed severe headache, blurred vision, chest pain, nausea, and vomiting. She had marked mydriasis, tremor and BP and HR were 180/110 mmHg and 74 beats/minute, respectively. Intravenous lorazepam (2 mg) was given without improvement followed by phentolamine (2 mg). Her symptoms and BP markedly improved within minutes of phentolamine administration. Repeat doses of phentolamine were administered for recurrent and symptomatic hypertension over the next 24 hours. Urine drug screen confirmed presence of amphetamine and comprehensive screen of urine and serum showed dexamfetamine.
Discussion: Lisdexamfetamine is a prodrug metabolized to dexamfetamine *in vivo*.[1] Peak drug concentration (Tmax) of dexamfetamine occurs at 3 hours with therapeutic dosing. Dexamfetamine has a half-life of 10 hours. Previously reported ingestions have had standard sympathomimetic effects including tachycardia, hypertension, mydriasis, and flushing/sweating. Our patient showed primarily alpha-1 agonism-related effects: mydriasis and hypertension without tachycardia. Phentolamine, an alpha-1 antagonist, has been used to treat toxicity from drugs such as phenylpropanolamine, an amphetamine analogue with very high affinities for the alpha-1 receptor. The half-life of elimination of phentolamine is 19 minutes. Repeated doses (up to 5 mg for adults/2–4 hours) are often required when used as an antidote to treat alpha-1 agonist-related toxicity.
Conclusion: We present a case of lisdexamfetamine overdose resulting in hypertensive emergency treated successfully with phentolamine.

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257. Impact of an emergency short stay unit on emergency department performance with toxicology patients

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Objective: Different approaches have been suggested for inpatient management of toxicology presentations. A previous study showed that a multidisciplinary inpatient service decreases length of stay (LOS). The aim of this study was to investigate the impact of opening an emergency short-stay unit (ESSU) on emergency department performance for admitted toxicology patients.
Methods: This was a before and after study in a hospital with a tertiary toxicology service. An ESSU was opened in 2010. We compared the characteristics and LOS in patients presenting in the calendar years 2009 and 2012. Toxicology admissions were extracted from the toxicology clinical database and linked to the emergency department (ED) admissions database. Patients admitted to the intensive care unit (ICU) were excluded. Age, sex, triage category, and ED LOS were extracted from the databases. Study outcomes were ED LOS and the proportion of patients remaining in the ED for the duration of their admission.
Results: In 2009, there were 928 toxicology admissions of which 49 went to ICU and 879 were planned inpatient ward admissions. In 2012 there were 876 toxicology admissions of which 39 went to ICU and 837 were planned inpatient admissions. The two groups had similar demographics and triage categories (Table 1). The median ED LOS was 2.85h (interquartile range[IQR], 1.6–5h) in 2012 which was significantly shorter than a median ED LOS of 8.75h (4.8–14.1; $p < 0.00001$) in 2009.
Conclusion: The opening of ESSU improved performance of the ED in managing toxicology patients by decreasing their length of stay in the ED.

258. Acute poisonings admitted to the emergency department: Epidemiology and criteria of admission to the intensive care unit

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Objectives: In France, each year, approximately 150,000 poisoned patients are admitted to the emergency department (ED). Recent

Table 1. Demographics and triage categories.

	2009	2012
Number of ward Admissions	879	837
Females	538 (61.1%)	517 (61.8%)
Age (median; range)	33y (14–88y)	35y (16–96y)
Triage category (median)	Category 2*	Category 2
Emergency LOS	8.75h (0.5–45h)	2.85h (0.02–63h)
Proportion staying in ED	65.9%	7.5%

*Category 2 is an emergency

data regarding epidemiology are rare. Our objectives were to describe the epidemiology of such poisoned patients and investigate the criteria for admission to the intensive care unit (ICU).
Methods: Retrospective descriptive study from records of poisoned patients admitted to the ED of a university hospital in France, from January 2009 to December 2012. Predictive factors for ICU admission were obtained by mutivariate logistic regression analysis with the determination of odds ratio (OR) along with their 95% confidence intervals. Data are expressed as median (25–75 percentiles) or percentage as required.
Results: During 4 years, 882 poisoned patients (38 (26–47) years, 1M/3F) were admitted to the ED, representing approximately 1% of the total referred patients. Poisonings were mainly multidrug exposures (53%). The involved drugs included benzodiazepines (73%), selective serotonin–reuptake inhibitors (SSRI, 16%, 152 cases), acetaminophen (13%), neuroleptics (12%), sedative drugs like imidazopyridines, (9%), polycyclic antidepressants (0.9%, 8 cases), and cardiotoxicants (2%, 18 cases). Ethanol was present in 20% of the poisonings. Patients were discharged directly from the ED or after a < 24-h stay in the ED hospitalization unit (55%), were admitted to the psychiatric ward (29%), to a medical ward (3%) or to ICU (5%) and ran away from the ER (8%). Among patients admitted to the ICU, 25% were mechanically ventilated and one patient died. Predictive factor of ICU admission were cardiotoxicant exposure (OR, 7.2; CI95, 2.05–18.50) and Glasgow coma score (OR, 1.45; CI 95, 1.20–1.65 per point lost below a value of 10).
Conclusion: Acute poisonings represent a frequent cause for admissions to the ED. Psychotropic drugs represent the most frequently involved drugs in ED poisonings with an increasing incidence of SSRI. ICU admission remains rare and motivated by the nature of toxicant (cardiotoxicant) and coma depth.

259. Treatment of boric acid poisoning in two infants with continuous venovenous hemodialysis

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Objective: Boric acid poisoning in children is a relatively frequent single-substance intoxication mainly concerning children < 5 years of age.[1] After oral ingestion, boric acid is rapidly absorbed and distributed in tissues (low distribution volume), with highest concentrations occurring in brain and liver. It is excreted in urine with a mean half-life of 21 hours. Treatment consists of rapid elimination of the absorbed substance, and dialysis is part of the available elimination techniques. We report two cases of boric acid intoxication after accidental ingestion of an aqueous saturated solution. Both patients were treated with continuous venovenous hemodialysis (CVVHD)
Case series: Case 1: A 5.5 kg three-old-month infant, referred to our pediatric intensive care unit (PICU) 9 hours after accidental ingestion of 3.6 g of boric acid with moderate dehydration, tachycardia, tachypnea, and anuria. After rehydration and persistent oliguria, CVVHD was started 14 hours after the toxic ingestion. CVVHD was performed for 36 hours, with elimination of 767.4 mg of boric acid in the dialysate (k_d mean: 28.8 mL/min) and a decrease in serum boric acid levels from 257 to 2.1 micrograms/mL. Case 2: A 3.5 kg 40-day-old infant, was transferred to our PICU 12 hours after last ingestion of boric acid, wrongly administered in the milk for 3 consecutive meals (approximately 9 g) in the previous 24 hours. Rehydration resulted in increased urine output. In this case, CVVHD was started approximately 21 hours after the last meal and it was continued for 38 hours with a boric acid elimination in the dialysate of 213.9 mg (k_d mean: 15.1 mL/min) and a reduction of blood levels from 171.6 to 4 micrograms/mL.
Conclusion: In both cases, it was not possible to determine the total amount of boric acid excreted by urine. However, the contribution of dialysis to boric acid elimination is to be considered elevated, given the high clearance. The patients were discharged from the PICU on 7th and 9th day of hospitalization without important clinical problems. In conclusion, CVVHD is a suitable and efficient elimination technique in infants intoxicated with boric acid.

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260. Successful treatment of angiotensin-converting enzyme inhibitor angioedema with fresh frozen plasma

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Objective: Angiodema is a well-recognized adverse effect of angiotensin-converting enzyme (ACE) inhibitors. Severe cases may compromise a patient's airway. The condition is due to increased levels of bradykinin and not due to histamine, and standard treatment for allergic angioedema such as antihistamines, glucocorticoids and adrenaline is ineffective.[1] Several treatments have been empirically trialled for severe or persistent ACE inhibitor angioedema, including Icatibant[1], C-1 inhibitor concentrate[2], and fresh frozen plasma (FFP)[3] with reportedly more rapid resolution of symptoms as compared to historical controls. We report the case of a patient with ACE inhibitor angioedema successfully treated with FFP.
Case report: An 87-year-old man with a history of hypertension, Parkinson's disease, and dementia presented to the emergency department where evaluation revealed normal vital signs and physical examination with the exception of severe tongue edema. The patient had been taking enalapril for years and had no itching, urticaria, or other signs of allergic reaction. Suspected ACE-inhibitor induced angioedema was

treated with two units of fresh frozen plasma. The patient was discharged 4 hours after receiving treatment with symptom resolution.
Conclusion: Although most cases of ACE-inhibitor angioedema can be managed by discontinuing treatment, severe cases may benefit from treatments that decrease levels of circulating bradykinin. Until controlled studies have demonstrated the efficacy of any of the treatments, availability, off-label use restrictions, cost and side effects will guide the use of treatments. In favor of FFP is a lesser cost and widespread availability while the disadvantages of FFP are delayed time until administration, risk of volume overload, and transmission of infectious disease. In this patient, rapid discharge was possible after receiving FFP.

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261. Procedural safety in high-dose insulin euglycemia therapy by adoption of a target-controlled infusion regimen

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Objective: High-dose insulin euglycemia therapy (HIET) is an efficient therapy in life-threatening intoxications with calcium-channel blockers; hypoglycemia may be one of the serious side effects. We report the implementation and safe use of a target-controlled infusion protocol for glucose substitution in HIET.
Methods: We perform HIET by administration of insulin (1 U/kg body weight (BW) bolus and 1 U/kg/h infusion), accompanied by a continuous infusion of glucose at 0.15g/kg/h and of potassium. Before implementing HIET at our intensive care unit (ICU), we developed a target-controlled regimen, linking measured levels for blood glucose (BG) to infusion rates of parenteral glucose supplementation. We prespecified 3 different levels of values for BG, triggering different therapeutic interventions to keep the BG level around our target level of 150 mg/dL. BG controls are scheduled in a timetable (not shown), beginning with short intervals (5–10 minutes), incrementing while the BG remains stable and diminishing again in case of BG falling below definite limits (calculations aided by a computer-based algorithm): Limit 1: $120 < BG < 150$ mg/dL: raise infusion rate of glucose by 20%, next BG-control in 20 minutes; Limit 2: $80 < BG < 120$ mg/dL: apply bolus of 100 mL glucose 10%, raise infusion rate by 20%, next BG-control in 10 minutes; Limit 3: $BG < 80$ mg/dL: bolus of 200 mL glucose 10%, raise infusion rate by 40%, next control in 5 minutes.
Results: After adopting this scheme, a male patient (17 years, 70 kg BW) was admitted with an intoxication with up to 3600 mg diltiazem, ingested 1 hour before. We started HIET as described, the patient suffered from vasoplegic shock without signs of heart failure. Besides standard therapy for shock, we administered a total of 1588 E of insulin and 900 g glucose within 27 hours. The minimal value of BG was measured at 82 mg/dL, the maximum 285 mg/dL. The patient left the hospital 3 days after admission without sequelae.
Conclusion: Besides the undisputed benefits, HIET bears a considerable risk for patients because of the enormous amounts of insulin applied; furthermore, it poses a considerable workload and stress for the medical staff. Prespecified protocols are helpful and may be recommended in this risky situation.

262. Procedural safety in lipid rescue therapy for various intoxications by adoption of a protocol defining indications and application

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Objective: Lipid rescue therapy (LRT) is standard therapy in life-threatening intoxications with local anesthetics. Growing experience supports its use in intoxications with various (antiarrhythmic, antihypertensive, neuroleptic, and antipsychotic) drugs. The acuteness of severe intoxications, associated with the workload generated by the deteriorating clinical state of the patient, poses considerable stress for the medical team. We report the implementation and safe use of a protocol defining indications and guiding procedures in LRT.
Methods: The potential of a drug to be temporarily removed from circulation by LRT is directly related to its positive oil/water solubility coefficient (pKa). On this basis, we investigated the drugs of our catchment area and considered them as candidates for LRT if their pK(a) was around 2 or higher. We compiled a database of 87 drugs and limited the use of LRT to life-threatening intoxications with drugs mentioned within. Furthermore, we developed a protocol guiding the staff through LRT, beginning with checking indication and presence of life-threatening intoxication, continuing with initial diagnostic procedures including laboratory studies and leading to the initiation of LRT, which is performed according to the otherwise published standards for therapy of local anesthetic toxicity. The calculations are aided by a computer-based algorithm. The procedure ends with a follow-up check 24 hours after termination of LRT.
Results: In the last 3 years, we have treated 6 patients with LRT according to our protocol. In all cases, life-threatening intoxication was present and the adherence to the protocol was thorough. The performing physicians reported good guidance by the protocol and stressed the advantage of having a predefined procedure at hand.
Conclusion: Considering the complex clinical setting in treating severely intoxicated patients, a standardized protocol with well-described indications and procedures may be helpful, especially regarding the rareness of these events, even in specialized centers.

263. Necessity of early carboxyhemoglobin determination in carbon monoxide poisoning

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Objective: Although the value of carboxyhemoglobin blood levels (CO-Hb) for the assessment of poisoning severity and prognosis is disputed,[1] recommendations for medical treatment of carbon monoxide (CO) poisoning are often based on CO-Hb[2]. As CO-Hb can decrease rapidly, the value of early CO-Hb detection and usefulness of portable pulse-CO-oxymeters are examined.
Methods: (A) In patients with severe fire smoke poisoning CO-Hb-values determined on site by pulse-CO-oxymetry were requested by questionnaire from emergency medical services and compared with laboratory results from simultaneously drawn blood samples. (B) In patients with similar exposures, peak CO-Hb values detected during prehospital medical treatment (determined either by pulse-CO-oxymetry or from blood sample analysis) are compared with results of the initial blood gas analysis after hospital admission (requested by questionnaires from hospitals).
Results: (A) In 6 cases with CO-Hb-levels of 20, 12, 11, 7, 6, and 1%, the maximum difference was 2.4% (absolute).[3] (B) In 21 cases with peak CO-Hb-levels between 5 and 57% (median: 35%), a decrease in CO-Hb between 14 and 85% (relative) of the peak value was observed (median: 51%). In 14 cases, the time elapsed could be determined exactly. The calculated elimination half-life times ranged between 57 and 194 min (median: 99 min).[3]
Conclusion: CO-Hb levels detected on hospital admission have little value for the assessment of CO poisoning severity, prognosis, and decision about specific treatment (i.e., hyperbaric oxygenation). CO-Hb should to be determined soon after termination of exposure, since disappearance of CO from the blood is enhanced under the terms of intensive medical care, going along with the administration of high oxygen concentrations. Pulse-CO-oxymeters allow simple, rapid, and reliable measurement of CO-Hb in the preclinical phase.

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264. Lithium intoxications in patients on chronic therapy: Precipitating factors, management, and outcomes—2009–2012 experience of Milan Poison Control Centre

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Introduction: Lithium is the most widely used drug for prevention and therapy of bipolar affective diseases, and it is recommended as the first-choice mood stabilizer in most recent guidelines. Lithium therapy, however, is associated with many risks and difficult management, mainly because lithium has a narrow therapeutic window; lithium intoxication happens in between 75% and 90% of patients on maintenance therapy. This article aims to analyze circumstances, management, and outcomes of patients on chronic therapy affected by lithium intoxication without errors in drug taking. Acute events in chronic intoxication may happen in a patient on chronic therapy who has taken an intentional or unintentional overdose.
Methods: The Milan Poison Control Centre (PCC) analyzed all the calls related to unintentional lithium intoxications (overdose and adverse drug reaction) from January 1, 2009 to December 31, 2012. Several follow-ups in order to gather demographic, clinical, and laboratory data were collected; contributory causes to the intoxication, therapies and outcomes were recorded. The severity of clinical cases has been classified according to Hansen and Amdisen Scale.
Results: Milan PCC took from its own archives 153 cases of lithium intoxication in patients on chronic therapy, without errors in drug taking. These cases represent 24% of consultations recorded by the Milan PCC for intoxications due to lithium-containing drugs. We realized that 14% of these cases were asymptomatic; 44% had mild symptoms, such as nausea, tremors, asthenia; 34% had moderate symptoms, such as sopor, stiffness, and hypertonia; 8% had serious symptoms, such as coma, seizure and cardiovascular collapse; 5 patients with serious symptoms died. We have detected renal failure, vomiting, and nausea as precipitating factors in a large number of our cases.
Conclusion: Lithium intoxications in patients on chronic therapy are an important fraction of Milan PCC's consultations; precipitating diseases, mainly gastroenteric, have often been detected. The management of lithium base must be closely followed and with strict surveillance. Physicians have to inform patients correctly about drug interactions and possible precipitating factors.

265. Inefficacy of extracorporeal life support in four cases of acute colchicine poisoning: A preliminary report

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Objective: Colchicine poisoning may result in life-threatening organ failure, including the early onset of cardiogenic shock and the later onset of acute respiratory distress syndrome (ARDS). Consequently,

extracorporeal life support (ECLS) has been proposed in acute colchicine poisonings. We report failure of arteriovenous ECLS (ECLSav) in four cases of colchicine-induced cardiogenic shock.
Case series: Register of acute colchicine poisonings admitted to our intensive care unit since 1977. Prognostic factors were looked for twice daily over 96h post-ingestion. Indication for ECLS was set owing to the onset of cardiogenic shock refractory to betamimetic agents. Arterial and venous cannulae were set using a surgical procedure already reported. ECLSav was performed using the Rotaflow® Jostra-Maquette device with oxygenator Quadrox PLS. Results are expressed as median (extremes) or percentage.
Results: Since 2003, 6 patients have received ECLS, including 4 patients for colchicine-induced cardiogenic shock, and two additional patients who received venovenous ECLS for severe ARDS; the latter two patients were not included. The study group included 4 women, median age: 25 (17–49) years. The median supposed ingested dose: 50 mg (40–80) [0.93 (0.6–1.36) mg/kg]. The median delay in presentation to hospital: 6h50 (1h00–25h36). The median of the maximal measured white blood cell (WBC) count: 27,500/mm^3 (18,100–33,510), occurring 27h43 post ingestion (25h16–29h18), the median of the minimal PT: 11% (8–14), occurring 72h26 post ingestion (37h38–81h04). ECLSav started with a median delay of 53h51 post ingestion (32h55–77h00). Refractory cardiac arrest occurred in two patients. The median duration of ECLSav was 45h37 (73h40–94h00). The four patients died. The time to death from ingestion was 91h (73h40–154h42). The median of the latest measured white blood cell count during the course of the poisoning was 450/mm^3 (100–4600).
Conclusion: Inefficacy of ECLSav may have resulted from too late indication. Indeed, two patients received ECLS while being in refractory cardiac arrest. Conversely, ECLS may have delayed time to death. As a matter of fact, evidence of bone marrow suppression in peripheral blood was noted in the 4 patients. Therefore, we are presently refining prognostic factors.

266. Acute metformin overdose: Metformin serum concentrations during treatment

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Objective: The antidiabetic drug metformin is known to cause potentially lethal intoxications.[1] Metformin overdoses are reported frequently. Metabolic acidosis caused by metformin is commonly treated by hemodialysis, but only limited evidence is available for evaluation of effectiveness of dialysis to enhance metformin elimination.
Case report: We report on the case of a 40-year-old man who claimed to have ingested 65 grams of metformin together with alcoholic beverages in a suicidal attempt. He developed a peak serum lactate level of 10.2 mmol/L and a serum pH of 7.22. The initial serum metformin level was 145 mg/L (therapeutic range: 0.6–1.3 mg/L), ethanol 840 mg/L. After 3-h hemodialysis treatment (CVV-HDF) pH had increased to 7.39 and serum metformin level had decreased to 24.1 mg/L. In the following course, metformin serum levels were determined to be 5.7 and 2.1 mg/L after 7 and 14h, respectively.
Conclusion: Hemodialysis treatment compensates metabolic acidosis and seems to enhance metformin elimination. Even severe overdoses can be treated without sequelae.

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267. Methanol poisoning in Tasiilaq, Greenland

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Objectives: We present a case of potentially severe methanol poisoning in a resource-limited area. Blood sample analysis was limited, the specific antidote, fomepizole, was not available, and ethanol for infusion, beyond the available stock, could not be delivered by air due to aviation transport restrictions, nor by ship due to the presence of sea ice until 7 months after the incident.
Case report: A 53-year-old male was hospitalized after drinking 1 litre of "Origonol", a field kitchen fuel, containing 60–100 w/w% ethanol and 5–10 w/w% methanol. He was inebriated (s-ethanol unavailable) but awake and communicative. He was in a hypertensive state and had elevated liver parameters (Table 1). Poison centre recommendations included fomepizole, blood monitoring (electrolytes, anion gap, liver and renal functions, and serum ethanol), and consideration of dialysis. However, in Tasiilaq only limited laboratory equipment was available. One litre of pure ethanol for intravenous use was the only available antidote, and the nearest dialysis facility was 700 km away across the ice cap. Intravenous ethanol treatment was initiated, 50 grams as a bolus in 30 minutes—to theoretically reach a serum ethanol concentration of 100 mg/dL (21.7 mmol/L)—followed by a maintenance dose of 8 grams ethanol/hour. Vital parameters, focusing on respiratory frequency and urinary pH, were monitored every 2 hours for the evaluation of acidosis development (Table 1). Ethanol infusion was discontinued after 72 hours. The patient left the hospital on his own initiative the following day.
Conclusion: On follow-up, 2 days after the patient left hospital, the patient was well and had no visual disturbances. Tight monitoring of only a few basic parameters supported our patient's full recovery.

268. Lithium poisoning in the intensive care unit: A descriptive study and analysis of the predictive factors of hemodialysis

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Table 1. Monitoring of respiratory frequency and urinary pH in the Tasiilaq methanol poisoning case.

	Submission	IV ethanol initiation, Time, 0 hr	Time, 8 hr	Time, 24 hr	Time, 34 hr	Time, 72 hr
Respiratory frequency, min^{-1}	–	–	24	24	18	18
Urinary pH	–	5.5	5.5	6.5	7.0	8.5
Blood pressure, mmHg	143/84	159/74	133/76	135/69	108/70	149/82
Pulse, min^{-1}	117	106	117	102	100	118
Oxygen saturation, %	93	90	90	96	95	94
AST, U/L (normal range, 10–40 U/L)	323	–	–	216	153	99

Objective: Hemodialysis is the treatment of choice for severe lithium poisoning. However, despite increased lithium clearance, features are not always improved. Our purposes were 1) to describe lithium-poisoned patients admitted to the intensive care unit (ICU), 2) to assess poisoning impact on renal function, and 3) to identify predictive factors for dialysis in lithium poisoning.

Methods: We included all lithium-poisoned patients admitted to our ICU over 20 years (1992–2012). Renal function was assessed according to the RIFLE classification (Risk, Injury, and Failure; and Loss, and End-stage kidney disease). Results are expressed as median (interquartile range) or percentages when appropriate. Univariate analysis was performed using Mann–Whitney, t-student, and chi-square tests, as appropriate. Significant variables at a 5% threshold in the univariate analysis were entered in a stepwise multivariable logistic regression model.

Results: One hundred and forty-four lithium-poisoned patients (88F/56M; 45 [33–75] years; SAPS II: 31 [19–46]) were included. Lithium intoxication patterns were as follows: acute poisoning (10%), acute-on-chronic poisoning (65%), and chronic overdose (25%). The ingested dose was 15 g [5–24] with extended-release lithium formulation (65%) and polyintoxication (52%). Delay between poisoning and admission was 8 (4–28) hours. Glasgow coma score was 13 [10–15] on admission and the worst value 6 [3–12]. Complications included aspiration pneumonia (33%), shock (17%, predominantly vasoplegic) and seizures (8%). Lithium concentration on admission and peak were 2.3 [1.3–3.7] mmol/L and 2.8 [1.7–4.9] mmol/L, respectively. Management included whole bowel irrigation (25%), mechanical ventilation (40%), and dialysis (15%, 12 cases with intermittent dialysis, 6 cases with continuous hemofiltration, and 4 cases with both techniques). ICU length of stay was 4 [2–9] days. Four patients died (2 asystoles and 2 nosocomial infections). Admission, worst, and discharge creatinine concentrations were 87 [70–140] µmol/L, 96 [72–171] µmol/L and 59 [39–70] µmol/L, respectively. After hydration, 24-h urine output was 1.2 [0.7–1.9] mL/kg/h. According to the RIFLE classification, patients presented kidney failure (11%), kidney injury (8%), and kidney failure (10%). No patients developed end-stage renal disease. By multivariate analysis, lithium concentration of >3 mmol/L was the only predictive factor of dialysis (odds ratio, 5.6; 95% confidence interval, 2.5–25.2).

Conclusion: Lithium poisonings are rare but frequently associated with altered kidney function. The decision for hemodialysis is mainly based on lithium concentration.

269. Fat emulsion therapy given intraosseusly in massive verapamil overdose

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Objective: Intravenous fat emulsion (IFE) therapy is widely used in treating various medication overdoses. The standard route to administer IFE therapy is intravenously. We report on a patient receiving IFE through the intraosseus (IO) route. We also discuss difficulties in administering this route.

Case report: A 24-year-old female presented to the emergency department (ED) following a deliberate overdose. The patient reported taking approximately 30 tablets of 240 mg extended release verapamil along with a smaller but unknown quantity of 80 mg immediate release verapamil. The ingestion occurred 1–2 hours prior to arrival. On arrival, the patient's heart rate remained in the 80s but she was persistently hypotensive. The systolic blood pressure quickly dropped as low as 65/30. Following initial treatment, and no change in blood pressure, a decision was made to start both vasopressors and IFE therapy. Central access was established, and a norepinephrine drip was started. IFE was brought to ED, but peripheral access was lost at that time and not able to be reobtained. An IO line was then placed in left proximal tibia using an EZ-IO system. Good flow was noted through the IO line, and it was flushed with lidocaine prior to use. IFE was then started through IO. The patient was noted to report some pain with the infusion of the bolus. Half way during the bolus administration, the intravenous pump (Alaris brand) began to alarm that infusion was not flowing adequately. The pharmacist at the bedside noted that the pump could not administer the bolus rate through the required filter and then through the IO line. At this point, peripheral access was obtained and IFE infusion was moved to that site. The patient was admitted to the ICU and expired two days later.

Conclusion: A brief literature search revealed a report of IFE being given via the IO route to rats in bupivacaine-induced toxicity, but no human reports could be found. This case report illustrates a novel way of administering IFE therapy and potential complications that may arise in future administration.

270. Gastric lavage after overdose of large size slow release drugs

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Objective: The indications for gastric lavage are nowadays very restricted, but the procedure can still be considered when there has been a recent massive intake of highly toxic substances. Standard commercially available lavage tubes most commonly have a size of 32F with end- and side holes of 7 mm in diameter. Slow-release tablets or capsules are becoming increasingly common on the market. These preparations often remain in their original shape during prolonged periods throughout the gastrointestinal passage. The tablet/capsule size and disintegrating characteristics can therefore influence the possibility of removing the ingested preparations by gastric lavage.

Methods: Pharmaceutical properties (e.g., size, release characteristics) concerning selected slow-release drugs exceeding 7 mm in size were provided by drug pharmas. These data were used to estimate the possibility of extracting the tablets through a common size gastric lavage tube within 2 hours of the ingestion. The most common slow-release formulations available on the Swedish market of the following substances were chosen: carbamazepine, diltiazem, iron, lithium, metoprolol, potassium, propranolol, quetiapine, tramadol, valproate, venlafaxine, and verapamil. All these drugs can cause very serious symptoms following a substantial overdose.
Results: In our study, three of the twelve investigated drugs, venlafaxine (Efexor depot), metoprolol (Seloken Zoc), and propranolol (Inderal retard) can be expected to dissolve within 2 hours after the ingestion. The remaining nine preparations disintegrate at a slower rate. The design of several of these drugs will also keep the size and shape of the tablets unaltered throughout the gastrointestinal passage.
Conclusion: Gastric lavage, with conventional standard gastric tubes (32F), is most likely ineffectual for the removal of several important slow-release drugs, based upon tablet/capsule size and other pharmaceutical properties. Although systematic clinical observations or experimental investigations are needed to confirm these conclusions, use of a larger lavage tube or alternative methods for elimination of slow-release drugs should be considered. Whole bowel irrigation can be a preventive option when serious symptoms are expected to occur.

271. Gastric decontamination in poisoned patients operated for bariatric surgery

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Objective: The number of patients who have undergone surgery for obesity is increasing, and occasionally they present at emergency units due to acute overdosing of pharmaceuticals. This has created a need for poisons centers to outline practical guidelines for initial treatment of these patients. The general indications for gastric lavage are currently restricted, but the procedure can still be considered in special circumstances where there has been a recent, potentially lethal, intake of highly toxic substances.
Methods: All telephone inquiries to the Swedish Poisons Centre involving overdoses in patients operated with gastric bypass surgery were analyzed during a 6-month period in 2013.
Results: Nineteen patients (age span, 23–68 years) were registered and females dominated (16/19). Gastric lavage was performed in four cases with very poor result. In one of these patients, the procedure caused a minor gastric bleeding. Activated charcoal was given in several instances without any apparent complications. Whole bowel irrigation was used in two cases (lithium and iron overdose).
Discussion: There are several different surgical methods available, but globally, gastric bypass by far seems to be the most preferred technique. All methods substantially reduce the functional size of the gastric remnant. This implies that the anatomical conditions for a successful gastric lavage are lacking. Furthermore, there is a risk that the large bore tube will cause perforation injuries to the blind gastric pouch created by the surgery. The ingested pills will rapidly be distributed into the jejunum and hence be inaccessible to extraction by a gastric tube. There is no room for the fluid volumes normally used in the gastric lavage procedure. Therefore, the risk of regurgitation and subsequent aspiration to the lungs also increases.
Conclusion: Gastric lavage is not indicated in a patient who has undergone gastric bypass surgery. Activated charcoal can be given, but divided into small portions of less than 100 mL. Whole bowel irrigation can be considered in exceptional cases where large amounts of toxic slow-release preparations have been ingested. If accessible and judged relevant, an abdominal computed tomography (CT) may provide valuable diagnostic information and help guide treatment option.

272. Epidemiology of acute poisoning in children admitted to the emergency department of the Institute of Mother and Child of the Republic of Moldova

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Objectives: To study children with acute intoxication admitted to the emergency department of the Institute of Mother and Child.
Methods: We carried out a retrospective study of child poisoning cases admitted to the emergency department between September 1, 2011 and September 1, 2013, using the following criteria: gender, age, etiology, and severity of acute poisoning.
Results: Nine hundred and seventy-six children with acute poisoning were included, representing 4.9% of total patients with medical emergencies. The proportions by the age are the following: children up to 1 year, 36 (3.6%); 1–5 years old, 527 (53.9%); 5–12 years old, 112 (11.4%); and 12–18 years old, 301 (30.8%). The etiology was the following: medicines 341 (34.9%); household substances 304 (31.1%); alcohol 165 (16.9%); psychoactive substances 44 (4.5%); mushrooms 41 (4.2%); carbon monoxide 26 (2.6%); new psychoactive substances 22 (2.2%); hydrocarbons 12 (1.2%); mandrake, hyoscyamus 11 (1.1%); nitrates 7 (0.7%); and rodenticides 3 (0.3%). Regarding the severity of poisoning, the cases were classified as follows: mild poisoning, 511 children (52.3%); medium, 298 children (30.5%); and severe forms, 167 children (17.1%).
Conclusion: The main cause of poisoning in children is represented by medicines, followed by household products and alcohol: data similar to the literature.[1] There are two peaks of implicated age: between 1–5 years and during adolescence.

Reference

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273. Launch of a new BfR App "poisoning accidents among children"

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Objective: Around 200,000 calls are received annually at the nine poison information centres (PCs) in Germany. Approximately half of the cases involve children. Parents suddenly confronted with a potential poisoning of their child often act in panic, sometimes even aggravating the situation. The Federal Institute for Risk Assessment (BfR) has therefore developed a new app called "Poisoning Accidents among Children" to help parents and child carers in emergencies.
Methods: In the well-arranged design of the app, all substances have been listed in alphabetical order and assigned to different categories, for example, household products, medicines, and plants. The articles on these products provide information about potentially toxic ingredients, possible symptoms, and appropriate first-aid measures. The contents were based on the long experience of consultancy by German PCs, first published in a BfR brochure "Risk of Poisoning Accidents Among Children" in 2008.
Results: In the general part of the app, typical poisoning scenarios and possible precautions are described. To provide fast medical advice by experienced toxicologists in an emergency, a direct link to the hotlines of all nine German PCs has been installed. The BfR app was developed for Smartphones (operating systems Android/iOS). Since its launch in August 2013, it can be downloaded in app stores free of charge. Once installed, the app can be used even without a direct Internet link. During the first 3 months, the BfR app has been downloaded 87,000 times and rated to be easy to use and very helpful by most users. The requests of some users to integrate more plants and mushrooms or to adapt the app also to the Windows operating system will be implemented soon.
Conclusion: The new BfR app offers rapid information and a direct link to the 24h service of PCs in actual and suspected cases of poisoning. By informing parents about hazardous products in everyday life, accidents can be prevented. Thus, the BfR app not only provides help in cases of emergency but is above all intended to contribute to reducing the number of poisoning accidents among children in the future. First steps have been taken to provide an English version.

274. Childhood poisoning in Sweden: A twenty-year perspective

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Objective: To describe the Swedish pattern of poisoning in children during 2010 and to compare it with the results observed 10 and 20 years earlier.
Methods: Case records from Swedish hospitals concerning poisoning in children < 10 years of age during 2010 were analyzed retrospectively and graded according to the Poisoning Severity Score (PSS).[1] Data from the Swedish Poisons Information Centre (PC) statistics of inquiries and from the Swedish national inpatient register were also analyzed. The results were compared with equivalent data collected 10 and 20 years earlier.
Results: According to the official national statistics, 465 children < 10 years were hospitalized in Sweden with a diagnosis code of poisoning during 2010. The PC received 272 case records regarding children < 10 years who were treated in hospital due to a poisoning accident the same year. Most of the children were in the age group 1–3 years. The poisonings were caused by pharmaceuticals (44%), chemical products (41%) and plants, mushrooms, or snake bites (15%). Most children developed none or mild symptoms, 22 children (8%) developed moderate symptoms, and severe poisonings were rare, with only in 5 cases (2%). This pattern is the same as observed in analyses performed in 1990 and 2000. Between 1990 and 2000, the number of hospitalized children due to poisoning accidents decreased by one-half and between 2000 and 2010 by one-third. During the latter period, the number of inquiries to the PC has been approximately at the same level regarding cases in this age group.
Conclusion: The number of children < 10 years in need of hospital care due to poisoning continues to decrease and serious poisonings are uncommon in Sweden. It is suggested that the Swedish PC has had an important role in this positive trend through preventive work with authorities and manufacturers and by information to the public. Moreover, the availability of a more comprehensive and quality assured database regarding consequences of accidental exposures in children has reduced the need for hospitalization as a precautionary measure.

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275. Prospective follow-up study on battery ingestion in children younger than 6 years

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Objective: Although 80–90% of all ingested batteries pass the gastrointestinal tract without any problems, recent literature suggests that the number of severe and fatal button battery ingestions is increasing. Severe complications have been reported after ingestion of lithium-type button batteries, large diameter cells (≥ 20 mm) and in children < 4 years.[1] Consequently, the current recommended treatment strategy in case of (suspected) battery ingestion is to send all children < 6 years to hospital for urgent radiographic localization. Battery diameter is described as a major predictor for the development of significant clinical symptoms.[1] The current recommendations may therefore be too cautious and lead to unnecessary referral and costs. In order to get better insight into the risk factors for battery ingestion and the health effects involved, the Dutch Poisons Information Center (DPIC) is performing a prospective follow-up study on battery ingestion in children < 6 years.
Methods: From October 2011 to August 2013, all consecutive cases of battery ingestion in children < 6 years, about which the DPIC was consulted, were included for follow-up. Follow-up was performed via telephone by using a standardized questionnaire.
Results: One hundred and seventy-five patients were included. Button battery ingestion was confirmed in 108 patients (62%). Battery diameter was known in 75 patients (69%). Fifty-three patients ingested batteries < 15 mm (49%), and 22 patients ingested batteries ≥ 15 mm (20%). In 5 patients, the ingested

button batteries (all ≥ 15 mm) were localized in the oesophagus. All were endoscopically removed. The relationship between the diameter and the location of the ingested battery was significant (Fisher's test; $p < 0.001$). No cases of severe complications were reported.

Conclusion: As oesophageal batteries pose the greatest risk for serious complications, the diameter of the battery can be used to identify those patients requiring an urgent X-ray. When selecting high-risk patients on the basis of battery size, the need for radiographic localization in children can be decreased by at least 49%, leading to a reduction in costs. However, as this follow-up study continues, final conclusions cannot yet be drawn.

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276. Infant botulism treated with equine botulinum antitoxin: A case report

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Objective: Infant botulism (IB) results from absorption of botulinum neurotoxins (BoNTs) produced *in situ* by Clostridia colonizing the intestinal lumen and is reported in infants less than 1 year.[1,2] BoNTs induce skeletal muscle paralysis by producing a presynaptic blockade to the release of acetylcholine.[3] The clinical onset is insidious and characterized by constipation, difficulty in sucking, progressive weakness, and difficulty in breathing.

Case report: A 5-month old baby was admitted to the pediatric department for constipation, difficulty in sucking, and weak cry. Medical history was negative for perinatal or delivery complications and symptoms were started after hexavalent vaccine administration. During the hospitalization ptosis, strabismus, mydriasis, lethargy, and weak muscular body control were noted. The patient received corticosteroids, antibiotics, fluids, and antiviral therapy. Clinical course improved quickly, and the baby was discharged 7 days later. During the programmed follow-up (10 days later), constipation and difficulty in sucking and feeding were documented. Further investigation revealed that the child had ingested homemade honey: IB was suspected. Analytical determinations confirmed clinical diagnosis of botulism, as *Clostridium botulinum* type A was detected in rectal swabs, while honey samples resulted negative. At the suggestion of Rome Poison Control Centre (PCC) and in agreement with Pavia PCC, Trivalent-Equine-Antitoxin (TEqA, 750 IU-anti-A, 500 IU-anti-B, 50 IU-anti-E per mL; 10 ml/kg in 2 hours) was administered. The patient was transferred to the pediatric intensive care unit and his clinical conditions quickly improved. After 1 month, the baby was discharged without sequelae.

Conclusion: This case report highlights: i) the difficulty in an IB diagnosis as it is a rare and little-known syndrome with subclinical onset, ii) the necessity of thorough training and awareness of physicians and pediatricians, iii) the safety of TEqA in IB treatment, iv) honey is not the main vehicle of BoNTs producers. In this case, indeed the most likely source of intoxication was the dust settled on the clothes of baby's father who works as a bricklayer.[4]

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277. Characteristics of severely poisoned children admitted to the tertiary pediatric intensive care unit: A shift from organophosphate poisoning to corrosives

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Objective: To compare poisonings in children admitted to the paediatric intensive care unit (PICU) before the changes in legislation regarding the use of pesticides and thereafter.

Methods: Retrospective analysis of patient's data from 1982 to 2003 and computer data base analysis of admissions from 2004 to 2012 from a level III multidisciplinary PICU, which admits patients from 0 to 14 years. Patients were classified into two groups: early group (1982–2003) and late group (2004–2012). The division between the two was based arbitrarily on the time of implementation of the Plant Protection Products Act (2004), which changed the availability of pesticides on the Slovenian market.

Results: Eighty-six poisoned children were admitted to our PICU from 1982 to 2012: 61 before 2004 (2.7 per year) and 25 (2.8 per year) thereafter. The median age (range) was similar in both groups: 39 months (18–169) in the early group and 45 (2–220) in late group (Wilcoxon test; $p = 0.9394$). Children in the early group were poisoned by organophosphates (28), sedatives (12), ethanol (4), gasses (3), mushrooms (2), gasoline (2), corrosives (1), other drugs (8), and others (1). Children in the late group were poisoned by sedatives (2), ethanol (5), gasses (1), mushrooms (1), snake bites (2), corrosives (8), other drugs (4), and others (2). A difference between distribution of poisoning by organophosphates and corrosives in both groups was statistically significant (chi-square test; $p < 0.0005$). Mechanical ventilation was needed in 53 (87%) children in the early group and in 17 (68%) in the late group; central venous line was inserted in 44 (72%) and 11 (44%); and inotropic/vasopressor support was started in 37 (61%) and 2 (8%), respectively. The level of intensive care was significantly reduced from late to early group (chi-square test;

p = 0.0254). Four children died in the early group and all children in late group survived (chi-square test; p 0.4873).
Conclusion: Concurrently with the new legislation causing a decrease in dangerous pesticide availability in Slovenia, we noticed a dramatic reduction in the number of poisonings by organophosphorus insecticides, with an increase in poisoning with corrosives. Although the admission rate remained constant, the severity of poisoning in children decreased.

278. Levothyroxine: Acute toxicity in newborns

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Objective: Levothyroxine (T4) is given therapeutically in infants with hypo- or athyroidism in doses of 10–15 micrograms/kg/d. In healthy infants, it is sometimes given inadvertently instead of a vitamin D-preparation. The aim of this study was to determine the acute toxicity of levothyroxine in overdose in newborns younger or equal to 28 days old, since information is limited.
Methods: A multicenter retrospective review of acute levothyroxine monointoxications involving infants < 28 days reported to German, Austrian, and Swiss poison centres (PCs) with follow-up at least 24 hours later or without follow-up in symptomatic patients.
Results: Fifty-four newborns were included. Gastrointestinal decontamination with charcoal was performed in 1 patient. Mild symptoms were reported in 12/54 cases (22%; Table 1). Observed symptoms were restlessness or agitation (6 cases), increased respiratory rate (1 case), and diarrhoea (3 cases, mostly the day after). One child was reported to have lost weight (3.9 → 2.8 kg) observed on day 3. This child was lost to follow-up and was not well documented.
Conclusion: 78% remained asymptomatic and 22% developed mild symptoms. A slight dose-relationship was observed. Although many drugs have a relatively high toxicity in newborns because of the immaturity of many organ-systems levothyroxine seems to have a large margin of safety probably because of the high need for this hormone during the first weeks of life. Postnatally both T3 and T4 serum concentrations increase fourfold to sixfold within the first hours and gradually decline to adult values over the first 4 weeks of life.

279. Development of respiratory acidosis following the ingestion of a liquid detergent capsule by a boy aged 1 year 10 months: A case report

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Table 1. Dose ingested, severity, and outcome.

Dose	Number of cases	Asympto-matic (%)	Mild (%)	Moderate (%)	Severe (%)	Unclear (%)
< 30 µg/kg	36	30 (87)	6 (13)	0	0	0
> 30 < 50 µg/kg	14	9 (79)	4 (21)	0	0	7 (1 Fall)
> 50 < 60 µg/kg	4	3 (75)	1 (25)	0	0	0

Objective: Water-soluble laundry detergent capsules (LDC) are laundry products containing highly concentrated cleaning agents. In Estonia, LDCs became widely available in 2012. The Estonian Poisoning Information Centre (EPIC) has received 43 inquiries concerning LDC exposure during the period January 1, 2012–November 1, 2013. The majority of inquiries concerned unintentional exposures in children 5 years of age or less, except for one intentional exposure concerning a 16 year old. Exposures mainly occurred as "ingestion only". Ingestion may result in gastrointestinal complaints, chemical burns, respiratory problems, acidosis, and altered state of consciousness. The aim of this report is to describe development of acidosis due to ingestion of LDC by a toddler.
Case report: A boy aged 1 year 10 months who had swallowed about half of an LDC was admitted to the Children´s Clinic of Tartu University Hospital (CCTUH) at 03.03.2013. At admission there were no aberrations in clinical findings. The child was hospitalized for observation. A few hours later, the child developed hyperthermia, hyperglycaemia, acidosis, dyspnoea, and airway secretion. Moist rales were auscultated bilaterally. Acetaminophen, ibubrofen, and amoxicillin were administered. By the next morning, the patient's condition had deteriorated: respiratory rate 50x, SpO_2 86–90%, heart rate 161x, and acidosis worsened. On X-ray aspiration pneumonia was detected. EPIC was consulted. The patient was transferred to the paediatric intensive care unit (PICU). Additional oxygen was started, prednisolone intravenously and salbutamol inhalations were administered. The amoxicillin treatment was changed to intravenous ampicillin administration. As a result of the treatment, ventilation improved and acidosis was corrected. The child had no appetite, and drank minimally. The child started to eat and drink adequately 06.03, but had difficulty ingesting hard food. Patient was discharged on day 7. Follow up on 11.03.2013: minimal cough and minimal findings on chest X-ray persisted.
Results: 03.03.2013 pH 7.289, pCO_2 40.6, glucose 15.2 mmol/L; 04.03.2013 pH 7.359, pCO_2 33,9, lactate 3.1 mmol/L, glucose 7.2 mmol/L C-reactive protein (CRP) 36 mg/L; X-ray: aspiration pneumonia; 09.03.2013: CRP 3 mg/L, white blood cell 9.3 E^9/L.
Conclusion: Due to the increased risk of aspiration pneumonia, acidosis and chemical burns, children with exposure to LDCs should be referred to hospital for evaluation even in the case of mild initial symptoms. Greater consumer awareness is required to reduce injury from LDC.

280. Characterization of the use of naloxone in pediatric patients using data from the Toxicology Investigators Consortium

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Objective: In 2009, American College of Medical Toxicology (ACMT) established the Toxicology Investigators Consortium (ToxIC). This network was constituted to promote multicenter research in toxicology and enable the nationwide collection of important toxicological data from patients at the bedside. We used the ToxIC database to investigate characteristics of pediatric patients receiving naloxone over 1 year. Research Question: What are the characteristics of patients age 18 years and younger that received naloxone?
Methods: We searched the ToxIC database for all cases of patients who received naloxone from October 1, 2012 to September 30, 2013. Patients aged 18 years and younger were examined and divided into four groups: age < 2 years, 2–6 years, 7–12 years, and 13–18 years. Patients were evaluated for sex, type of exposure, and indication for naloxone administration and specific xenobiotic implicated.
Results: Five hundred and fifty-seven patients were recorded as given naloxone during the study period. Sixty-eight (12.2%) of patients were 18 years and younger; of these, 14 (2.5%) were < 2 years, 17 (3.1%) were 2–6 years, 4 (0.7%) were 7–12 years, and 33 (5.7%) were 13–18 years. The number of males was greater than that of females in all groups except the 7–12 year group (males = females). For ages < 2 years, 2–6 years, 7–12 years, unintentional pharmacologic exposure was associated with receiving naloxone in 85.7%, 88.2%, and 50% of cases, respectively. Patients of 13–18 years had 0.0% unintentional pharmacologic exposures. Patients received naloxone for coma and/or respiratory depression in 78.6% for the < 2 year group, 76.5% in the 2–6 year group, 100% in the 7–12 year group, and 60.6% in the 13–18 year group. The proportion of xenobiotics associated with naloxone administration in each age group was calculated. The most common xenobiotics associated with naloxone administration were buprenorphine (17.7%), oxycodone (13.2%) and clonidine (11.8%).
Conclusion: The prescription opioid abuse epidemic results in increased availability of opioids in the home. The ToxIC database shows that naloxone use in children is mostly due to unintentional pharmacologic exposures which supports this. The most common xenobiotic implicated was buprenorphine. According to the ToxIC database, the most common cause for naloxone administration in the pediatric population was unintentional pharmacologic exposure.

281. Accidental ingestion of paliperidone (Invega R) in children: A case series

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Objective: To describe 3 cases of accidental ingestion of paliperidone in children between the age of 2 and 6 years.
Case series: Case 1. A 2-year-old girl was brought to the emergency department (ED) 2 hours after accidental ingestion of 6 slow-release 9 mg paliperidone tablets. Clinical examination was normal on admission. After a few hours, the child became somnolent, tachycardic (170/min), and quickly lost consciousness. She was transferred to the intensive care unit (ICU) and immediately intubated. Extubation was possible after 48 hours. She recovered uneventfully. Case 2. A 6-year-old boy was admitted to the ED for apathy and confusion of unknown origin. After a lumbar puncture and a computed tomography (CT) scan the child was transferred to another hospital. On arrival, he presented somnolence, confusion, hypertonia (upper limbs in flexion, lower limbs in extension), slight neck stiffness, body temperature of 37.4°C, and tachycardia 155/min. Diagnosis of one slow-release 6 mg paliperidone tablet ingestion was made because the child's sibling arrived in the first hospital with similar symptoms and the history of paliperidone ingestion (see case 3). The child was observed in the ICU and the symptoms resolved in 24 hours. Case 3. A girl, 4 years old, sister of case 2, was admitted in the ED for sleepiness and confusion, a few hours after her brother. Her parents found a blister of slow-release 6 mg paliperidone tablets in her pocket, 2 tablets were missing. On admission, she presented hypotonia, confusion, miosis, and tachycardia 140/min. The child was observed during 24 hours. The symptoms resolved gradually.
Conclusion: Paliperidone, an active metabolite of risperidone, can cause serious intoxications in young children. Because of the slow-release formulation, the first symptoms appear a few hours after ingestion and can suddenly become life threatening as in case 1. Delayed life-threatening cardiovascular symptoms were also described by Levine et al.[1] in a case of voluntary ingestion of paliperidone by a 14-year-old girl.

Reference

1. Levine M, Lovecchio F, Tafoya P, et al. Paliperidone overdose with delayed onset of toxicity. Ann Emerg Med 2011; 58:80–2.

282. A poisoning prevention program aimed at adolescents in Wales: Is it needed?

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Background: Paediatric poisoning has a bimodal distribution. Most cases occur in children < 5 years old with a second peak > 12 years. Exposure in the first group usually involves accidental poisoning.

Poisoning prevention in this group has been widely studied with only a few poisoning prevention interventions being considered successful. Harborview Injury Prevention and Research Center (HIPRC) looked into best practices of poisoning prevention and found little value in community and physician-based educational programs in reducing poisoning in children. Reducing pack sizes and implementing child-proof containers have proved effective. These measures were aimed at children under 5 years. Exposure patterns in adolescents are different, mainly taking substances in two ways: recreational abuse or to self-harm. Educational initiatives aimed towards decreasing the recreational abuse of drugs in this group are available within Wales. However, whilst some charitable organizations aim to prevent youth suicide, there is little focus on poisoning as a means of self-harm.

Objective: Review statistics from AWISS (All Wales Injury Surveillance System) and UKPID (United Kingdom Poisons Information Database) involving cases of poisoning in Wales, focusing on trends in age and gender. From these results, to look at developing a trend-focused educational program for adolescent children, focusing on deliberate self-poisoning for children aged 11–19.

Results: The AWISS data from 2009 to 2012 show that in Wales, emergency attendances to hospitals due to poisoning were greater in adolescents than in young children. Twenty-nine per cent of attendances involved children (0–4 years), 55% involved 15–19 years, and 10% those aged 11–14 years. In the age range 0–4 years, the distribution between sexes is even; in the 11–14 and 15–19 year age ranges, 67% and 62% of attendances were female. UKPID data show that there are more calls regarding females in the age groups 11–14 and 15–19 years (60% female to 40% male for both age groups) whereas in children < 5 years it is evenly distributed.

Conclusion: An education program aimed at the prevention of adolescent poisoning needs to be considered in Wales. This program, while highlighting the role of substances used to self-harm, should be aimed at adolescents, and consideration should be given to the gender balance involved.

283. A review of pediatric cases exposed to unknown xenobiotics

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Objective: Pediatric cases reported to poison centers (PC) often involve a pill that is unable to be identified. The outcome of pediatric exposures to unknown xenobiotics has never been studied and, currently, there are no standard recommendations regarding management. The objective of this study was to describe the demographics, poison center recommendations, and outcomes in the pediatric patient who may have ingested an unknown xenobiotic.

Methods: The electronic database at one US poison center, representing a population of 2.5 million, was queried from January 1, 2003 to October 15, 2013 for unknown drug exposures using the American Association of Poison Centers generic code 0077980. Records were restricted to children under the age of 6. Cases were individually reviewed and demographics, caller location, PC recommendations, disposition, and outcome were recorded.

Results: The search resulted in 286 cases, of which 108 were excluded as the exposure was actually identified. Of the remaining 178 cases, the average patient age was 2.7 years. The distribution was even between male and female. Of the 76% ($n = 136$) of the calls that originated from the child's home, 65% ($n = 99$) were referred to a health care facility (HCF). When referred to a HCF, 41% ($n = 41$) followed the PC recommendation and were evaluated at the HCF. Guidance to health care providers regarding the 66 patients evaluated in a HCF included: average observation time of 5.5 hours, administering activated charcoal (13.6% of cases), and obtaining an electrocardiogram (ECG) (13.6% of cases). Acetaminophen and aspirin levels were advised in 24.2% and 24.8% of all cases, respectively, while electrolytes and blood glucose testing were recommended approximately one-fifth of the time. Eight patients were admitted, of which six remained asymptomatic. The other two patients were documented to have "minor effects" and were asymptomatic following overnight observation. No patient was symptomatic 24 hours later.

Conclusion: There were practical variations in recommendations over a 10-year period given to providers of pediatric patients with an unknown exposure; however, the PC tended to recommend HCF evaluation and observation. While there was a limited follow-up, there were no reported long-term effects from these exposures.

284. Suicide attempt and suicide by medication poisoning in children and adolescents: Moroccan Poison Control Centre data

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Objective: Suicide is the second leading cause of death for those aged between 10 and 24 years. Poisoning is one of the preferred means of committing suicide.[1] In Morocco, there is a lack of data about self-poisoning among young people. Thus, we have conducted a study to analyze patterns of suicide and suicide attempts by medication poisoning in children and adolescents reported to the Moroccan Poison Control Centre (CAPM) for the purpose of improving prevention.

Methods: A retrospective study from January 2000 to December 2008 was conducted including all medication self-poisoning cases in children and adolescents reported to the CAPM. The age classification used was the International Programme on Chemical Safety classification, and the drug classification was Anatomic Therapeutic Chemical.

Results: Over the eight-year period, 1568 cases of suicide attempts by medication poisoning in children and adolescents were reported. Patients were from urban origin in 91.7% of cases. The average age was 16.4 ± 0.7 (9–15) years, and 80.5% cases were adolescents (15–19 years). Females comprised 83.2% ($p < 0.001$). In addition, the highest frequency of cases occurred from May to October (48.3%). The drugs implicated in the largest number of poisoning cases were nervous system drugs (63.1% of cases) with anxiolytics being the most common (55.7%). The mortality rate was 0.6% (7 deaths). Age 15 years or more, and poisoning with cardiovascular and musculoskeletal system drugs were the risk factors for death.

Conclusion: Female adolescents are most affected by suicidal drug poisoning, and the mortality rate is higher. A prospective study including other toxic poisonings, and psychological and socio-demographic characteristics of adolescents is needed to determine the risk factors for suicide attempts and to establish a prevention program.

Reference

1. World Health Organization: Suicide prevention web release. Geneva, Author, 2008. http://www.who.int/mental_health/prevention/suicide/suicideprevent/en [accessed 15 Nov 2013].

285. A case of inadvertent ingestion of cinacalcet by a 1-year-old child

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Objective: Cinacalcet is a drug that diminishes calcium in patients with carcinoma of the parathyroid glands or primary hyperparathyroidism or in end-stage renal disease with secondary hyperparathyroidism. We report a case of inadvertent paediatric ingestion.
Case report: A 1-year-old girl accidentally took one 30 mg Mimpara® pill (cinacalcet). Approximately 1.5 hours after the ingestion, she started to vomit and became lethargic. On the advice of the poison centre, they went to the nearby hospital. On admission, she was falling asleep repeatedly. When being woken up, she started to cry and was agitated. The other clinical parameters were normal. A blood gas analysis on arrival showed an ionized calcium of 1.16 (1.15–1.29) mmol/L with a pH of 7.30 (7.38–7.42) and a lactate of 2.4 mmol/L (<1.3). It is known that an acidosis can raise the calcium and the actual calcium could be lower. The poison center advised repeated calcium levels. A serum analysis 2 hours after ingestion showed a total calcium of 2.33 (2.20–2.70) mmol/L with a slightly elevated total protein of 75 (54–70) g/L. An infusion of calcium-gluconate was started. Serum analysis 6 and 19 hours after ingestion showed a total calcium of 2.18 and 2.25 (2.20–2.70) mmol/L. The infusion of calcium was subsequently stopped. The girl left the hospital after 2 days in good clinical condition. Cinacalcet concentrations were determined in the serum samples at 2, 6 and 19 hours after ingestion. The results were respectively 129, 84, and <10 ng/mL (adult median peak value, single 25 mg dose: 7.22 ng/mL) [1].
Conclusion: To our knowledge, there are no published case reports of overdoses. Haemodialysis patients have been given doses titrated up to 300 mg daily (Mimpara SPC, 2013). The Swedish Poison Centre (Hultén P, personal communication) had a call about a 74-year-old woman who took an overdose of 420 mg cinacalcet, with an ionized calcium value of 1.16 mmol/L (1.14–1.32). She had no major symptoms. In our case, we saw a low calcium despite an infusion of calcium gluconate. Until more information is available, we advise close medical observation for any paediatric ingestion.

Reference

1. MICROMEDEX® Healthcare Series Vol. 158, 2013.

286. Pediatric dimetinden exposures

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Objective: There is a paucity of literature about pediatric dimetinden exposures. In general, toxicity occurs after ingestion of 3–5 times the usual daily dose. Children are more sensitive to the toxic effects of antihistamines than adults. According to the National Toxicological Information Centre in Bratislava, intoxications by dimetinden have an increasing tendency.
Methods: A retrospective analysis of calls due to overdose of dimetinden was performed, using the electronic records database from January 2003 to November 2013. The outcome was evaluated based on the telephone inquiries and discharge reports of hospitalized patients. One of the inclusion criteria was a single ingestion with a mg/kg dose calculated based on average weight for age.
Results: Of 194 cases, 98 cases of pediatric dimetinden ingestion met the inclusion criteria. Ages ranged from 3 months to 5 years. Most of these children (70.4%) were less than 3 years old and 53% were female. The amounts ingested ranged from 3 to 20 mg or 0.2 mg/kg–1.7 mg/kg. Fifty-seven (58%) children were hospitalized for 2–3 days, and seventeen (17%) were admitted for observation for several hours. The majority of children were asymptomatic; 46% of intoxications were accompanied by mild, transient, and spontaneously resolving symptoms (PSS1) only. Somnolence was observed only in children ingesting ≥ 0.4–0.7 mg/kg (4–6.5 times the maximum recommended daily dose). In children ingesting ≥ 0.7–1.7 mg/kg, mild effects were observed as follows: somnolence, tachycardia, mydriasis, excitation, hypertension, nausea, and vomiting. Severe dimetinden poisoning was not reported in this study.
Conclusion: In children ingesting ≥ 0.7–1.7 mg/kg (6.5–15 times the maximum recommended daily dose) only mild symptoms were observed. Based on our results, we assume that hospitalization of the exposed children for a few days is not necessary.

287. Exposures to liquid detergent capsules in children

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Objective: The Poisons Information Centre Erfurt has observed an increasing number of exposures to liquid detergent capsules since 2012, particularly in infants. We evaluated the causes and risks of these cases.
Case series: Between July 2012 and October 2013, 48 exposures in children and one in a puppy were reported. Children were aged 5 months to 5 years (median, 2 years). Immediate and recurrent emesis was the primary symptom in most cases (71.4%). In some cases, only retching appeared. Breathing difficulties such as coughing, hoarseness, and stertorous breathing also

occurred frequently (30.6%). Children with a definite exposure but without symptoms had only a short oral or dermal contact with the detergent solution without actual ingestion. Case: A 17-month-old male toddler probably ingested the total content of one Persil Duo-Caps® (combination of concentrated detergent with a bleaching agent). He spewed and vomited once at home. Recurrent emesis and diarrhoea began during clinical examination. Violent coughing and rhonchi occurred 30 minutes later. Leucocytosis and rise in C-reactive protein were noted. Chest X-ray showed a brochopneumonic pattern; therefore, the child was treated with antibiotics. Full recovery of breathing function was observed on the 9th day after exposure.
Conclusion: The attractive product design in a water-soluble envelope is the cause of an increasing number of exposures.[1] Due to the concentrated nature of the detergent, ingestion of even small amounts may cause intensive gastrointestinal disturbances in children. In contrast to other household detergent exposures, these cases are associated with a high risk of aspiration so immediate clinical admission is required.

Reference

1. Williams H, Jones S, Wood K, et al. Reported toxicity in 1486 liquid detergent capsule exposures to the UK National Poisons Information Service 2009 - 2012, including their ophthalmic and CNS effects. Clin Toxicol (Phila) 2014; 52:136–40.

288. Brain death and overdose

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Objective: High-profile cases published in scientific and lay literature suggest patients with sedative-hypnotic or other psychoactive overdoses may be at risk of premature diagnosis of brain death. We seek to determine prevalence of brain death discussion and diagnosis among fatal poisonings reported to a US Poison Center (PC).
Methods: Using cross-sectional methodology, two unblinded investigators coded all records involving brain death in patients > 18 years old from a regional PC between 1/1/03 and 6/30/12 using a data abstraction tool; a third person adjudicated discrepancies. Reported ingestions were categorized as presence/absence of psychoactive substances defined to include opioids, sedative-hypnotics, antidepressants, antipsychotics, and anti-epileptics. Time of presentation, initial brain death discussion reported to PC, and time of brain death diagnosis were recorded. Descriptive statistics were used for data analysis.
Results: There were 35 cases documented as suspected and/or diagnosed brain dead out of 259 deaths reported during the study period (13.5%; CI, 9.3%–17.7%). Thirty patients (86%; CI, 74.5%–97.5%) were documented within 3d of presentation and 13 (37%, CI 21%–53%) were suspected brain dead within 24h. Sixteen cases were documented brain dead by non-specified examination; eleven occurred within 3d and three occurred within 24h. Of cases declared brain dead within 3d, 5 ingested a psychoactive drug. Among the three patients declared brain dead within 24h, two had a documented psychoactive overdose (both were combination benzodiazepine and opioid).
Conclusion: The diagnosis of brain death leaves no room for error. Unique to psychoactive overdose, patients may mimic brain death (3–5 days) and go on to full neurologic recovery. A premature report of brain death to patients' families is inappropriate, yet in our cohort of patients, this occurred frequently. The two cases of psychoactive overdose diagnosed brain dead within 24h are of paramount concern. Withdrawing care when there is potential for complete neurologic recovery is reprehensible. This study only includes cases reported to PC, so prevalence of suspected brain death is underestimated. A prospective case–control study including injury severity and comorbidity scoring may help eliminate premature death assignments. Persistent intoxication must be considered before discussing brain death with family or initiating brain death examination on patients.

289. Cerebral injury in 2-chloroethanol intoxication

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Background: Cerebral microhemorrhages are recognized as a marker of microangiopathy and tend to be the diagnostic and prognostic implicators in vascular diseases of the brain. 2-Chloroethanol is a toxic solvent with an LD50 of 58 mg/kg orally in rats. Grape farmers in Taiwan apply it on grapevines to hasten sprouting and can land themselves in potentially lethal conditions. Severe intoxications are uncommon and can present with hypotension, respiratory failure, seizure, coma or death, occurring within 24 hours even after only skin or inhalational exposure. The toxic mechanism of 2-chloroethanol on the brain is not clear. Here, we report a farmer with 2-chloroethanol intoxication with typical findings of diffuse cerebral microhemorrhage on brain magnetic resonance imaging (MRI).
Case report: A 68-year-old farmer suffered from nausea, vomiting, abdominal pain, and shortness of breath which worsened to confusion, seizure, hypotension, and respiratory failure after 2-chloroethanol exposure for several hours. Nonocclusive mesenteric ischemia developed on the 3rd day and diffuse subcortical microhemorrhage found by MRI due to persisting consciousness change on the 13th day. The patient survived and was discharged with mild cognition dysfunction 36 days after intoxication.
Conclusion: The vascular injuries of this patient seemed to be consistent with the results of some earlier *ex vivo* studies. Chloroacetaldehyde, the metabolite of 2-chloroethanol catalyzed by alcohol dehydrogenase, might be the toxicological principle and play a decisive role in the systemic toxicity of 2-chloroethanol.

290. Premature diagnostic closure of metabolic acidosis and hypotension attributed to propylene glycol toxicity in a cirrhotic patient

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Objective: Describe a case of sepsis misattributed to propylene glycol toxicity.
Case report: A 59-year-old woman with hepatic cirrhosis, chronic obstructive pulmonary disease (COPD), morbid obesity, and recent hip replacement was admitted to the hospital for shortness of breath, hypoxemia, epigastric pain, hip pain, hypotension, and tachycardia. Upon diagnosis of bilateral deep vein thromboses, a heparin infusion was initiated and an inferior vena cava (IVC) filter was placed. Blood cultures were positive for methicillin-sensitive *Staphylococcus aureus* (MSSA) and Enterobacter. Given increasing pain in the recently replaced hip, she was taken to the operating room for hip washout and replacement. Intraoperative cultures were congruent with her blood cultures. Vancomycin and cefepime were continued postoperative, and the patient was later intubated for respiratory insufficiency complicated by acute respiratory distress syndrome. A lorazepam infusion was initiated for sedation. On post-operative day (POD) 2, she developed worsening acute kidney injury (creatinine, 2.2 mg/dL). By POD 6, she had received a total of 1049 mg of lorazepam with a concurrent load of 868 g of propylene glycol (PG) carrier. Her PG level was $>$ 100 mg/dL Based on her osmolar gap, her calculated maximum PG level was 249.4 mg/dL. Measured serum L-lactate was 3.8 mmol/L. Continuous venovenous hemodialysis was initiated on POD 13 for presumed PG toxicity. Despite aggressive therapy, the patient succumbed to sepsis and died on POD 18 due to an unidentified source of infection. Autopsy later revealed bacterial peritonitis.
Conclusion: PG toxicity can cause significant morbidity in the intensive care unit, especially among patients with renal and hepatic dysfunction. However, a concerted effort to rule out alternative causes of clinical deterioration should be made prior to attributing these effects to propylene glycol.

291. Fatal insulin overdose: Role of the clinical laboratory

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Objective: We present a case report of a fatality due to suicidal administration of insulin to illustrate the role of the clinical laboratory in identifying the agent responsible.
Methods: A 44-year-old male with a history of suicide attempts was found unconscious in his closed car in an empty lot. He had presumably been there for a few hours on a hot, sunny day. A pre-hospital team found him with a Glasgow coma scale of 11, temperature 38.4°C, blood pressure 130/75 mmHg, heart rate 80 bpm, capillary glucose 64 mg/dL and administered naloxone (1.4 mg), flumazenil (1 mg) and glucose with no response. He was intubated and transferred to our hospital with recurrent hypoglycemia requiring dextrose, and generalized seizures treated with benzodiazepines. Due to a suspected sulfonylurea overdose (his mother received treatment with insulin and glibenclamide), octreotide (initially 50 micrograms subcutaneously (SC), followed by 100 micrograms) as well as high doses of intravenous (IV) dextrose (more than 150 g in the first hour) were administered, as well as sedation, relaxation, and physical cooling measures. Abnormal blood test results at admission revealed a serum glucose of 8 mg/dL, creatine phosphokinase (CPK) of 2466 U/I, potassium 3.4 mEq/L, and 26,200 leucocytes. The result of chest X-ray, cranial computed tomography, and urine analysis were normal, and a spinal tap revealed a glucose of 15 mg/dL, with otherwise unremarkable results. Antibiotics were administered until results were available. The patient was admitted to intensive care where he received further sedation and mechanical ventilation and, after 12 hours of repetitive hypoglycemia despite high volumes of IV dextrose, requirements returned to normal with no further hypoglycemic events. The patient progressed to generalized cerebral edema and severe neurological sequelae, ultimately resulting in death 2 months later.
Results: Insulin levels measured approximately 16 h after presentation revealed 43.8 mcUI/mL (ref 3–25) and a C-peptide of 0.14 ng/mL (ref 1.10–4.40) by chemiluminescence immunoassay suggesting exogenous insulin administration. Further testing with urine and serum liquid chromatography and mass spectrometry confirmed the absence of glibenclamide (and other commonly prescribed oral antidiabetics).
Conclusion: We describe a case report of suicidal hypoglycemia where exogenous insulin was determined by the laboratory to be the responsible agent.

292. Acute heart failure after venlafaxine overdose: Post-mortem myocardial examination in two cases

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Objective: Venlafaxine (VEN) is a bicyclic antidepressant that may be associated with severe cardiotoxicity following large overdose.[1] There are few post-mortem descriptions of ultrastructural changes in the myocardium. We describe two cases, with also the determination of VEN and metabolite concentration in the cardiac tissue.
Case series: A 38-yr-old woman who had ingested 4.2 g of extended-release VEN developed cardiogenic shock 6 hours post-ingestion. The peak serum concentration was: VEN 2153.3 ng/mL and O-desmethylvenlafaxine (ODV) 960.1 ng/mL. A severe left ventricular failure was demonstrated at echocardiography. Related complications were acute renal failure, rhabdomyolysis, and ischemic liver injury. The patient was treated with major doses of vasopressors and inotropes. She died on day 11 from multiple organ failure following recent *S. pneumoniae* septicaemia. The heart microscopic examination revealed multiple foci of dissolution with degenerative changes of the myocardial fibres accompanied by dark micro-deposits and large quantities of granular deposits (also present in the proximal renal tubules). The following post-mortem tissue concentrations were noted: heart, VEN 18 mg/kg, ODV 21 mg/kg; kidney, VEN 5 mg/kg, and ODV 1.2 mg/kg. A 38-yr-old woman ingested an unknown amount of VEN and verapamil. The peak serum concentration was VEN 7135 ng/mL, ODV 3434

ng/mL, and verapamil 1205 ng/mL. She presented cardiogenic shock refractory to inotropes and vasopressors and died on day 7 from multiple organ failure. Myofibrillar degeneration and necrosis without inflammation were noted in the myocardium. Tissue concentration was VEN 50.6 mg/kg and ODV 74.2 mg/kg.
Conclusion: Degenerative and poorly inflammatory changes may be observed in the myocardium after fatal VEN overdoses with cardiotoxicity. As the patients usually required large doses of catecholamines, the ultrastructural changes may also be partly due to catecholamine-induced myocardial injury or to ischemic-hypoxic injury. Until now, post-mortem tissue concentrations of VEN were not reported for the heart. It appears from our observations that a significant amount of VEN and ODV can be found in the myocardium.

Reference

1. Batista M, Dugernier T, Simon M, et al. The spectrum of acute heart failure after venlafaxine overdose. Clin Toxicol (Phila) 2013; 51:92–5.

293. High clinical suspicion and prompt treatment are life saving in accidental cyanide poisoning in children

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Objective: Clinical manifestations of acute cyanide poisoning have been widely described in literature.[1,2] However, cases of childhood exposure to cyanide are rare and the diagnosis is difficult to make due to the nonspecific nature of the signs and symptoms of cyanide poisoning. We describe a case of accidental cyanide poisoning in an 11-month-old infant with complete recovery after cyanide antidote therapy.
Case report: An 11-month-old female infant presented in the emergency department with apnea, circulatory collapse, bradycardia, and central nervous system depression with a Glasgow coma scale score of 3–4. At the initial emergency call to the poison center, a potential exposure to a powder 30 minutes before the onset of symptoms, probably boric acid, was reported. This was stored in a house cupboard and powder residue was also found on her hands on pediatric intensive care unit (PICU) admission. Initial arterial blood gas showed severe acidosis (pH 6.88, CO_2 20, HCO_3 3.8), hyperglycemia (464 mg/dL) and a very high lactate concentration (above the measurable range of the blood gas analyzer). As clinical and laboratory assessment were not consistent with boric acid poisoning, a detailed history and home search was undertaken. This revealed that powder of a cyanide salt used by the girl's grandfather, a jewellery manufacturer who had passed away 13 years ago, was kept in a bedroom cupboard. Sodium nitrite and sodium thiosulfate antidotes were administered with parallel measurement of methemoglobin levels. After 2 hours of treatment, improvement in acidosis and a lactate reduction were confirmed on blood gas analysis (pH 7.261, lactate 7.5 mmol/L).The patient was extubated 7 hours after entering PICU, remained stable, and was transferred to the pediatric ward after 48 hours.
Conclusion: Because of its infrequent occurrence in children, diagnosis of cyanide poisoning might be delayed and could be fatal. It is therefore critical for health care professionals to be well versed in clinical manifestations of cyanide poisoning. A high index of suspicion together with the prompt availability of cyanide antidotes can be life-saving in such emergencies.

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294. Mefenamic acid toxicosis in dogs and cats: A consecutive case series

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Objective: Mefenamic acid (MA) is a fenamate nonsteroidal anti-inflammatory drug (NSAID) which exhibits central nervous system (CNS) toxicity in human overdose with seizures as a common manifestation. The aim of this study was to analyse the clinical features of MA poisoning in domestic animals, since information on patterns of MA toxicosis is scarce.
Methods: Retrospective consecutive review of MA poisonings in cats and dogs reported by veterinarians to our poisons center between June 1997 and May 2013 with written medical feedback on clinical course.
Results: Forty-six dogs and thirteen cats could be included. The ingested dose ranged from 10 to 900 mg/kg (mean 173). Twenty (36%) animals remained asymptomatic, 22 (37%) showed minor, 12 (20%) moderate, and 4 (7%) severe symptoms according to the Poisoning Severity Score. There was one fatality. The susceptibility to MA toxicity was similar in cats and dogs. In both species, minor symptoms occurred after ingestion of 20–428 mg/kg MA (mean, 186), moderate after 50–900 mg/kg (mean, 200), and severe after 38–166 mg/kg (mean, 118). Signs and symptoms predominantly involved the central nervous system (CNS), and 18 animals had isolated neurological manifestations (Table 1). The minimal dose for a single convulsive episode was 66 mg/kg in a dog and 50 mg/kg in a cat. Multiple seizures, apnoea, and death occurred in a cat after ingestion of 125 mg/kg.
Conclusion: Overdose was associated mostly with mild to moderate neurological and gastrointestinal toxicity. In contrast to other NSAIDs, the frequency of seizures was striking as it has also been described in humans. Poisoned dogs and cats should therefore be monitored for CNS symptoms.

295. The third lethal case over the last year with the weight loss agent 2,4-dinitrophenol

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Table 1. Symptoms and signs observed in the 59 included animals (cats and dogs).

Symptoms/ Signs	Severity			
	Minor n (%)	Moderate n (%)	Severe n (%)	Fatal n (%)
Ataxia	18 (30.5)			
Somnolence	6 (10.2)			
Tremor	8 (13.5)			
Myoclonia[1]	2 (3.4)	2 (3.4)		
Muscle cramps[2]		2 (3.4)		
Seizures[3]		7 (11.8)	4 (6.8)	
Agitation	1 (1.7)			
Miosis	1 (1.7)			
Hypersalivation	3 (5.0)			
Vomitus[4]	11 (18.6)		1 (1.7)	
Diarrhea[5]	1 (1.7)	2 (3.4)	1 (1.7)	
Tachycardia	1 (1.7)			
Hypothermia	3 (5.8)			
Apnoea				1 (1.7)

[1]minor: infrequent muscle jerks; moderate: frequent, generalized muscle jerks
[2]moderate: contractions of multiple muscles
[3]moderate: acute single convulsive episode, severe: repeated seizures
[4]minor: mild vomiting, severe: persistent vomiting with dehydration
[5]minor: mild diarrhea, moderate: diarrhea with presence of blood in the stool, severe: persistent diarrhea with dehydration

Objective: 2,4-Dinitrophenol (DNP) is a well-known weight loss agent from the 1930s and then abandoned since several deaths occurred. In the 21st century, the Internet availability created a revival of DNP use among bodybuilders and overweight, with more than ten deaths described in the literature. DNP uncouples the oxidative phosphorylation in cells leading to excessive production of heat instead of ATP, increasing the risk of progressive lethal hyperthermia. The Swedish Poisons Information Centre was involved in three fatal cases within less than a year (June 2012–May 2013).

Case report: A 23-year-old female ingested 84 tablets of 25 mg (= 2 g) of agomelatine and 2.2 g of 2,4-dinitrophenol, in addition to ongoing dietary self-treatment with 200 mg DNP daily for 1 week. She experienced breathing difficulties and was brought to hospital. In the emergency room, 5.5 hours post ingestion, she was awake, pale, sweaty and restless, and had dilated pupils with yellow discoloration of the sclera. She had tachycardia 165/min, blood pressure 150/80 mmHg, body temperature 38.5°C, dyspnoea and was brought to the intensive care unit. Diazepam 5 mg intravenously was given twice, but the heart rate increased to 180–190/min and temperature 39.5°C. Immediately after intubation, 6.5 hours post ingestion, electrocardiogram (ECG) showed wide QRS complexes and cardiac arrest ensued, cardiopulmonary resuscitation (CPR) was initiated. Pronounced muscle rigidity was evident and non-depolarizing muscle relaxants were used without effect. Extreme hyperkalemia was 11.9 mmol/L, lactate 20 mmol/L, and pH < 6.80. CPR was terminated after 30 minutes. An autopsy verified the presence of 2,4-dinitrophenol (13.6 microgram/g blood). The agomelatine overdose was not expected to give severe symptoms. Two additional lethal cases have recently been identified (post-mortem analysis showing 34 microgram/g blood in both cases) in Sweden indicating the need for physicians to recognize this potentially lethal intoxication at an early stage. Forensic analysis of DNP is not routinely performed so the true number of DNP deaths may be higher.

Conclusion: The narrow margin between desirable and toxic effects increases the risk of severe poisonings and despite intensive care the risk of deadly outcome is high. DNP poisoning should be considered when a patient presents unclear progressive hyperthermia.

296. Severe toxicity after use of 2,4-dinitrophenol reported to the UK National Poisons Information Service

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Background: 2,4-Dinitrophenol (DNP) was introduced as a weight-losing drug in the United States during the 1930s[1] but was banned as a result of serious adverse effects and fatalities[2]. DNP use has increased in popularity worldwide recently as an aid to weight loss[3], but severe toxicity and fatalities have been reported[4].
Objective: This study was performed to characterize the toxicity of DNP reported to the UK National Poisons Information Service (NPIS).
Methods: NPIS telephone enquiry records and user sessions for TOXBASE®, the NPIS online information database, involving systemic exposures to DNP were reviewed for the period January 1, 2007 to August 15, 2013.
Results: Of 23 exposures (20 males, 3 females; median age, 24 years) reported by telephone, there were 3 during 2007–2011, 5 during 2012, and 15 during 2013 (to August 15th). TOXBASE® user sessions also increased sharply from 6 in 2011 to 35 in 2012 and 127 in 2013. Exposure was reported as chronic (n = 15), acute (n = 6), acute on chronic (n = 1), and unknown (n = 1). Commonly reported features were fever (61%), tachycardia (57%), sweating (39%), skin discoloration or rash (35%), nausea or vomiting (22%), abdominal pain (17%), and headache (17%). Agitation, metabolic acidosis, and chest pain were each reported in 13% of cases. There were five (22%; 95% confidence intervals 8%, 44%) fatalities, three involving acute exposure.
Conclusion: There has been a recent increase in DNP exposures reported to the NPIS by telephone and in accesses to TOXBASE®, with a high mortality. Measures to improve public awareness are needed to warn potential users of the severe and sometimes fatal toxicity that may occur.

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297. Thyrotoxic periodic paralysis secondary to overuse of liothyronine

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Objective: Thyrotoxic periodic paralysis (TPP), a genetic condition causing diffuse muscle weakness in the setting of hyperthyroidism, is most commonly reported in males of East Asian and Southeast Asian descent. We present a case of TPP secondary to intentional unsupervised overuse of liothyronine (synthetic T3).
Case report: A 26-year-old man of East Asian descent presented to the emergency department with generalized weakness for 1 day. He denied pain, fever, sensory changes, trauma, travel, or unusual food exposures. The patient admitted to using liothyronine sodium 25 microgram tablets obtained via the Internet and not medically supervised in an attempt to lose weight. Two weeks prior to presentation, he increased the dose of the drug to four tablets (100 microgram) daily. Initial vital signs were normal. Physical examination was remarkable for strength of 4/5 in upper extremities and 2/5 in lower extremities with proximal muscle groups more affected than distal ones The patellar, biceps, triceps, and Achilles deep tendon reflexes were noted to be absent. The patient's mental status, cranial nerve, and sensory examinations were normal. Initial laboratory studies were Na^+ 140 mmol/L, K^+ 1.6 mmol/L, Cl^- 107 mmol/L, HCO_3^- 24 mmol/L, BUN 12 mg/dL, Cr 0.64 mg/dL, Ca^{2+} 9.5 mg/dL, Mg^{2+} 1.4 mg/dL, Phos 3.7mg/dL, creatine phosphokinase (CPK) 127 U/L, thyroid-stimulating hormone (TSH) 0.16 microIU/L, total T3 $>$ 1614 ng/dL, total T4 $<$ 0.25 ng/dL, and aldosterone 1.8 ng/dL. An electrocardiogram showed normal sinus rhythm at 87 beats per minute with prominent U waves. Computed tomography scan of the head was normal. The patient was admitted to the hospital, and he was noted to have returned to his baseline strength within 24 hours. Repeat thyroid studies performed on hospital day 3 are total T3 119 ng/dL, total T4 0.39 ng/dL, and T3 uptake 44.8%. The patient was discharged to home on hospital day 4.
Conclusion: The medically unsupervised abuse of synthetic T3 may precipitate TPP in genetically susceptible individuals. It is important for practitioners to know that synthetic T3 is available for purchase via the Internet and thus is available for abuse by individuals who may be unaware of the potential for serious adverse effects.

298. Misuse of the herbicide chlormequat as euthanasia agent in veterinarian practice, an emerging problem?

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Objective: We present two cases of lethal secondary intoxication of dogs after ingestion of parts of the body of animals euthanized with chlormequat.
Case series: Case 1. A dog died after licking the open wound of a horse euthanized with a double intravenous dose of 5 mL Stabilan® 750 (chlormequat 750 g/L) by a veterinarian. The open wound was a jugular incision, made to find out the cause of the horse's respiratory problems. Shortly after exposure, the dog developed vomiting, black diarrhoea, mydriasis, and tremor. The dog died 20 minutes after the first symptoms. Case 2. A border collie died 1 hour after eating the entrails (liver, kidneys) from the open abdomen (probably for autopsy purpose) of a lamb euthanized by an intravenous injection of 4 mL Cycocel® (chlormequat chloride 750 g/L). Quickly after ingestion, the dog started to vomit, developed convulsions and difficulties of breathing. The veterinarian reported bronchial hypersecretion, bradycardia, and shock. Symptomatic treatment was initiated but was unsuccessful.
Conclusion: Chlormequat chloride is a plant growth regulator marketed in Belgium under 8 different brand names. Although chlormequat poisoning clinically resembles that seen with anticholinesterase compounds, it is not an acetylcholinesterase inhibitor and atropine seems to worsen the situation.[1] These 2 case reports prompted us to perform a short inquiry among farmers and veterinarians. Our survey showed that the misuse of chlormequat to euthanize animals seems not to be unusual in the agricultural world. In the literature, we found no report of chlormequat intoxication in animals and scarce reports of chlormequat ingestion in humans.[2,3] We would like to draw attention to the misuse of chlormequat and the risk of life-threatening secondary poisoning. We find it important to collect and share data about this dangerous malpractice to get a clear grasp on the scale of the problem.

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299. A case of intentional oral intake of T61

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Objective: We present a case of a suicide attempt by oral intake of 75 mL T61.
Case report: In a suicide attempt, a 46-year-old male veterinarian ingested 75 mL of T61, a product used for euthanasia of animals. Ten minutes later, he was unconscious and rapidly went into cardiac arrest. His colleagues immediately initiated cardiac resuscitation. The emergency medical services arrived 20 minutes after ingestion. The victim was immediately intubated, and adrenaline was injected, which led to recovery of a heart rhythm. At the emergency department, a second adrenaline shot and vasopressors were needed to treat a second cardiac arrest. After contact with the poison center, Intralipid 20% and N-acetylcysteine (NAC) therapy was initiated. The patient remained haemodynamically stable and was extubated after 1 day. On day 3, a four-fold increase in ALAT and ASAT was

noticed and PTQuick was reduced to 42%. In the medical history, one can point out chronic alcoholism and a partial hepatectomy (post traumatic). NAC therapy was continued during 6 days at the intensive care unit. Subsequently, the patient remained in hospital for 2 days until normalization of the liver enzymes.

Conclusion: T61 (Tanax) is marketed in several countries and is available in 50-mL vials. Each mL contains 200 mg embutramide (general anaesthetic), 50 mg mebezonium (curare-like action), 5 mg tetracaine (local anaesthetic), and 0.6 mL dimethylformamide (DMF) as a solvent. By intravenous administration, the 3 active components exert an immediate depressive cardiovascular and neurologic action. In voluntary intoxications, the intravenous injection is the most dangerous. Due to its simplicity of use, the oral route is also reported. Depending on the dose, it can lead to coma and cardiorespiratory failure. DMF is metabolized to methylisocyanate (MIC), which is highly hepatotoxic. The hepatotoxicity appears with a delay (1 day to a few days). As MIC is detoxified by glutathione, early treatment with NAC should be considered to prevent liver damage subsequent to DMF exposure.

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300. Accidental peroral Veratrum tincture poisoning: A case report

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Objective: Aqua Veratrum is a natural medication for external use only. The constituents of this medication are an ethanolic tincture from the rhizomes and roots of the *Veratrum* species, also known as false hellebore.[1] The recommendations for its use are the treatment of skin parasitic diseases: pediculosis, scabies, and fleas. In Lithuania, accidental peroral poisonings occur because of very similar packaging to cardiac drops.

Case report: A 59-year-old woman admitted at 6 a.m. to the emergency department of Lithuanian University of Health Sciences Hospital Kaunas Clinics and hospitalized for observation in the nephrology department. Her main complaints were general weakness, breathing difficulties, and fingertip numbness. Case history: she felt discomfort in her chest and elevation of blood pressure early on that morning and asked her husband for cardiac drop medication. Tincture of Veratrum was taken by mistake because of very similar packaging. The nausea, vomiting, and abdominal cramps appeared shortly after. She arrived in hospital approximately 2 hours post ingestion. Her clinical examination in admission was normal; she was conscious, felt weakness, heart rate (HR) rhythmical, 72/min., and blood pressure (BP) 100/70 mmHg. Electrocardiogram (ECG) on admission revealed sinus rhythm (SR) and right bundle branch block (RBBB). Her clinical and biochemical blood tests were normal. She received an intravenous infusion of fluids and cardiovascular monitoring was started. Severe hypotension 70/40 mmHg and sinus bradycardia 44–45/min developed 4 hours later. A bolus of 0.5 mg atropine sulphate was given intravenously. The BP and HR rose to normal ranges (90/60 mmHg and 77/min. respectively). Cardiovascular monitoring was continued, and the hypotension and bradycardia episode repeated 4.5 hours later. Repeated bolus doses of atropine were given intravenously. She underwent inpatient observation for more than 24 hours, and no more episodes of cardiovascular disorders were observed. ECG findings: RBBB disappeared. The patient was discharged without any clinical, ECG or laboratory changes 30 hours post admission.

Conclusion: This case illustrates the possibility of delayed and the repeated nature of cardiovascular disorders in Veratrum alkaloids poisoning and demonstrates the importance of prolonged cardiovascular monitoring in such poisonings.

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301. Rare occurrence of arsenic hydride poisoning in children

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Objective: Cases of arsenic hydride (AsH_3) poisoning are rare and occur primarily in various sectors of the industries. We have registered no cases of this type of poisoning in children before. According to the references, toxic arsenic concentration in human blood range from 0.1 to 1.6 mg/L, in urine to over 0.1 mg/L.

Case series: Three children aged 12–13 years were admitted to various Moscow children hospitals with unexplained haemolytic anaemia. The case history revealed that when they walked in the park, they inhaled the gas from toy-balloons bought from a street seller. In 8–10 hours, they started complaining of weakness, nausea, headache, stomach ache, and dark urine. Then, jaundice developed quickly accompanied by reduction in red blood count to 2.5 min and haemoglobin to 73 g/L. At the same time, the skin and sclera became more yellowish; the liver enlarged, ALT and AST values increased by 3 times; total bilirubin reached 83–141 mmol/L (normal: 1.7–20.7 mmol/L). The urea was 26.6 mmol/L (normal: 2.8–7.2 mmol/L), creatinine 396 micromol/L (normal: 45–105 micromol/l). Proteinuria, erythrocyturia, and diuresis rate reduction were noted. The clinical symptoms and case history made it possible to suspect arsenic hydride poisoning. Chemical and toxicological examinations demonstrated arsenic concentration in patients' blood of 0.944–1.097 mg/L and in urine of 0.791–0.854 mg/L. The patients were transferred to the children's toxicological center where they underwent chelation therapy with sodium 2,3-dithiolpropanesulfonate (0.005 g/kg body weight twice daily) and haemodiafiltration (3 sessions every 24 hours). After the therapy, the patients' general condition improved; their biochemical blood parameters normalized. Diuresis and haemoglobin levels gradually restored. After the first haemodiafiltration session, arsenic blood

concentration fell to 0.128 mg/L and less: urine level, 0.325–0.175 mg/L. After the second haemodiafiltration session, no arsenic was found in the patients' blood; urine concentration of 0.125 mg/L was found in one patient. In 14 days, the patients were discharged from the hospital for out-patient observation.
Conclusion: Thus, a new source of chemical hazard has been identified; moreover, we are of the opinion that the combination of chelating agents (sodium 2,3-dithiolpropanesulfonate) and haemodiafiltration for children treatment has proven its efficiency.

302. Magnetic resonance imaging findings and follow-up in a case with full recovery after ethylene glycol poisoning

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Objective: The value of brain computed tomography (CT) scan within 24–48 hours after ethylene glycol (EG) poisoning has been highlighted in a few isolated cases[1] and haemorrhagic lesions of lenticular nuclei described on magnetic resonance imaging (MRI)[2]. We report the CT and MRI findings at the early stage and at follow-up in a case with full recovery after EG poisoning.
Case report: A 37-year-old male presented with a Glasgow coma score (GCS) of 3, flaccid tetraplegia and metabolic acidosis, 5 hours after drinking about a gallon of an anti-freeze product. The arterial pH was at 6.77, $PaCO_2$ at 26.5 mmHg, blood bicarbonate at 3.8 mmol/L, and blood lactate at 19 mmol/L. The calculated anion gap $((Na^+ + K^+) - (HCO_3^- + Cl^-))$ was 41.7 mmol/L, not completely explained by blood lactate. The initial plasma ethylene glycol (EG) level was 191 mg/L. The patient immediately received mechanical ventilation and an intravenous dose of fomepizole. Non-enhanced brain CT scan at hour 24 after ingestion showed marked brain edema, hypodensity of basal ganglia, thalami, and brain stem. Acute renal failure developed on the following day, necessitating repeated sessions of haemodialysis. Sedation was stopped at D2. At D5 and D7, the patient was noted as GCS 8 and 15, respectively. He was successfully extubated at D7. A cranial MRI on D3 after ingestion showed bilateral and symmetrical high signal intensities in basal ganglia, capsulae, thalami, midbrain, dorsal pons, and medulla on FLAIR and Diffusion and high ADC values, in relation with vasogenic edema. Clinical and MR follow-up showed complete recovery at Day 13 after ingestion.
Conclusion: In this case, MRI findings suggest that at the early stage of EG poisoning while receiving haemodialysis, haemodialysis, and antidotal treatment, brain lesions may be related to vasogenic edema that might be associated with a full recovery.

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303. Unsuspected source of accidental group carbon monoxide poisoning

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Objective: Carbon monoxide (CO) poisoning presents very non-specifically and its sources can be hard to determine.
Case series: Nine women were brought to the emergency department of the Republic Vilnius University Hospital complaining of palpitations, fatigue, sleepiness, nausea and vomiting, headache, dizziness, face flushing, and paresthesiae. These symptoms had been lasting for 3 days. All of them had been working in a used clothes distribution warehouse. Physical examination showed somnolence, tachycardia, heightened arterial blood pressure, and face flushing. Pyrethroid insecticides and formaldehyde were suspected as possible poisoning agents, as those were used in the process of handling the clothes. Later blood carboxyhemoglobin concentration was tested and it was elevated in all women. After extensive exploration, the source of poisoning was revealed—an internal combustion engine transportation machine was working inside the warehouse.
Conclusion: Warehouse workers' headache is an infrequently reported form of CO poisoning due to industrial exposure.[1] Carbon monoxide poisoning should be suspected in all group poisonings, especially those presenting with non-specific complaints and physical examination findings.

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304. When the clinical findings are confusing, and the chemical analyses misleading. A toxic gas event in Oslo

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Objective: In toxic gas events, identification of the toxic agent may be difficult. Results from handheld analytical devices are often relied upon, as the clinical features are often non-specific. We present an event of toxic gas exposure where the final result from advanced laboratory techniques was completely different from the initial assumptions based on handheld devices.
Case series: Four security personnel were exposed to a gas at a restaurant complex immediately after closing hour at 2 am, reporting a chlorine-like smell near a restroom. On admission,

all had symptoms of dizziness, nausea, abnormal belching, headache, mild dyspnoea, and chest pain. Two complained of memory loss. One had a blood lactate of 2.7; otherwise normal arterial blood gas (ABG) analyses on hospital admission. There were normal blood analyses, chest X-rays, electrocardiographies (EKG), and spirometries, except a slight obstruction in one. Based on the chlorine-like smell, hypochlorite or similar was initially assumed to be the agent. The fire department analysed at the scene with a handheld chemical analyser, alerting from the toxic industrial chemical library "hydride", which does not include chlorine or hypochlorite. Another handheld method was applied, indicating phosphine, consistent with the hit in the hydride library. Phosphine was then considered to be the toxic agent. The ventilation system in the restaurant complex automatically shuts down at 2 am and turns on at 7 am. Analyses after 7 am did not reveal any gas. As this was unexpected, the Norwegian Defence Research Establishment performed air sampling using Fourier-transform infrared spectroscopy with the ventilation system off. Although the spectrometric library automatically returned the pattern as phosphine, specific phosphorus tests were negative. Manual analysis of the spectral data was necessary and revealed ozone as the toxic agent. The UV-filter in the industrial kitchen extractor did not automatically turn off together with the ventilation; the produced ozone followed the path of least resistance into the restroom, and caused the toxic exposure.

Conclusion: Although easy to use and rapidly available, handheld gas-analysers have limitations and require competent interpreters and confirmation tests. Ozone caused abnormal belching as one of the most consistent symptoms in all the patients, not described before.

305. Development of a new methodology to harmonize information on pesticide-related poisoning exposures and to support comparable reporting from EU member states

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Objectives: The methodology reported here is aimed at enabling Member States (MSs) to gather comparable data on acute pesticide-related poisoning and to support rapid exchange of information on cross border health threats possibly due to pesticide exposure/contamination. This plan of activity was developed within the EU co-funded project "Alerting Reporting Surveillance System for Chemical Health Threats Phase III" (ASHTIII) since pesticides, i.e., plant protection pesticides (PPPs) and biocides, are easily available and widely used hazardous chemicals; their misuse can cause mass exposure, environmental pollution, and food contamination, some of them can be used as chemical weapons. Importantly, EU legislation already requires reporting from MSs on poisonous exposures, although standard rules for data collection and reporting have not yet been provided.

Methods: Regulation 2009/1185/EU, providing a harmonized classification of PPPs (Annex III), and Regulation 2012/528/EU, providing the biocidal products classification (Annex V), were used as a basis to build the pesticide classification and coding system.

Results: The resulting pesticide system is two dimensional. The first part identifies the intended use of the compound according to the commercial product category of use it is contained in. More specifically, a three digit code provides the following information: primary category of use, that is, PP/biocide, (first digit); secondary category of use (second and third digits), that is, Major Group for PPPs or Main Group-Product Type for biocides. The second part of the system is used for chemical grouping and to identify chemical compounds. This part is organized into two levels: level one (three digits) identifies chemical grouping, for example, pyrethrins/pyrethroids, organophosphates; coumarins; level two identifies the active compound by using its standard denominations and CAS registry number. The system has been tested on different National databases to identify, classify, and code exposures to soil sterilants, rodenticides, acaricides, and insecticides in particular pyrethrins/pyrethroids.

Conclusion: The ASHTIII project is mainly aimed at implementing Decision 1082/2013/EU. Nevertheless, the criteria adopted to standardize information on exposure to pesticides, that is, using the same classification system for both PPPs and biocides, can be further developed and applied to other categories of chemical agents and support a variety of requirements of EU legislation.

306. Development of chemical emergency risk management monographs as a tool for provision of standardized health care measures in chemical incidents with cross-border health threats in EU (ASHT III project)

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Objective: To develop standardized documentation for the clinical management of chemical exposures and casualties in incidents with potential cross-border risks in order to support the European Commission and Member States in the co-ordinated response to serious cross border chemical incidents with a public health impact.

Methods: The list of 120 high-risk toxic industrial chemicals, chemicals of public health concern and deliberate release agents identified in RAS-CHEM and ASHT I/II projects was formed to model the best practice advice for the management of patients of chemical exposure

using coded terminology in a harmonized multi-lingual approach. The Clinical Effects Profiles were developed using MedDRA terminology to enable multi-lingual translation of the symptoms for incorporation into RAS-CHEM and further application within the Toxidrome IT tool for the identification of chemical agents from the associated signs and symptoms. The information from best practice authoritative sources which are used on a regular basis by the Poisons Centres and Public Health Authorities was utilized, and the system of internal/external peer-review, quality assurance and version/template control was implemented within the development process.

Results: The expert consensus was achieved on the structure of chemical emergency risk management (CERM) sheets including 14 general areas relevant to the public health risk and medical management of chemical exposures/casualties in the case of a chemical incident with cross-border health threat. Two-direction approach, "toxic agent-oriented" and "human-oriented", was developed to apply CERMs in situations with both confirmed and unknown toxic agents. The information included in CERM sheets enables the public authorities, risk assessors/managers, and medical professionals to plan and coordinate both "on-field" measures (decontamination, isolation, evacuation, triage, first aid, etc.), and specific medical measures (treatment with antidotes, secondary elimination, monitoring equipment, intensive care unit facilities etc.). For the electronic template of CERM sheets, the Adobe PDF format was used to enable XML Export for data matching, transfer, and translation.

Conclusion: The CERM monographs developed in the ASHT III project have a potential to address the gaps in the risk communication, assessment, and management of chemical incidents with cross-border health threats that were identified in EU by former health security projects.

307. Aluminum phosphide poisoning in the Tunisian Anti Poison Center

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Objective: Aluminum phosphide is a fumigating pesticide used in the storage of cereals. Acute intoxication with this product is rare in Tunisia, but it is associated with high mortality. We relate two cases of aluminum phosphide poisoning (APP) whose outcome was fatal.

Case series: 1: A previously well 16-year-old girl presented 2 hours after ingestion of one tablet of aluminium phosphide mixed with watermelon. She was agitated, vomiting, and had severe epigastric pain with blood pressure 60/40 mmHg, pulse 110 beats/min, oxygen saturation 86% on air, and temperature 37.1°C. Arterial blood gases (ABG) on 10 L/min oxygen showed pH 7.02, bicarbonate 6.2 mmol/L PO_2 50 mmHg, PCO_2 30 mmHg. Chest X-ray showed bilateral pulmonary infiltrates and ECG showed a left bundle branch block. She was treated with intravenous colloid (1 litre Gelofusion over 30 minutes), 250 mmol sodium bicarbonate, and epinephrine (maximum 3 µg/kg/min). She was sedated, paralysed, intubated, and ventilated. Biological investigation showed a rise in blood creatinine (223 µmol/L), with elevated liver aminotransferases (AST and ALT > 10x upper limit of normal). The level of creatine phosphokinase was about 450 UI/L, hemoglobin was about 9 g/dL, and platelets about 120,000/mm^3. Subsequently she developed disseminated intravascular coagulation and adult respiratory distress syndrome. Despite supportive management, she died 3 hours after admission. 2: A 45-year-old patient who ingested voluntarily 3 tablets of aluminum phosphide was brought to our emergency department by her family 2 hours later for stomach pain, polypnea, and agitation. Blood pressure: 70/34 mmHg, heart rate 35 bpm, and cyanosis of fingers. Biological investigation showed pH 7.02, HCO_3^- 5 mmol/L, PCO_2 28 mmol/L PO_2 40 mmHg, lactate 9 mmol/L. The patient quickly presented an irremediable cardio-circulatory arrest.

Conclusion: In the absence of an antidote and a codified treatment, the mortality of APP remains very high in our country. Legislative and administrative measures must be taken to restrict its supply.

308. Laundry detergent pod causing esophageal and gastric injury in an adult

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Objective: Since its introduction into the United States in 2011, ingestion of laundry detergent (LD) pods has become an increasingly common source of morbidity and mortality in the pediatric population.[1,2] However, injury associated with ingestion of LD pods by adults has not been described in the literature. We report a case of esophageal and gastric injury in an adult who ingested a laundry detergent pod.

Case report: A 50-year-old man with a history of hypertension drank the contents of a Tide Pods LD pod, mistaking it for candy. He vomited immediately after the ingestion and developed repeated emesis over the next 6 hours. His efforts to eat or drink caused pain and more emesis. The patient presented to the emergency department 12 hours after the ingestion, complaining of mild dysphagia. He had stable vital signs and an unremarkable examination, including a normal oropharynx, lung, and abdominal exam. An intravenous proton-pump inhibitor (PPI) was administered. An esophagogastrodoudenoscopy (EGD) performed in the emergency department revealed diffuse grade 2A esophageal injury, as well as erythema and ulcerations of the gastric mucosa. He was managed with a PPI, liquid diet, and discharged from the hospital the following day.

Conclusion: Despite the absence of physical examination findings, this adult patient had appreciable esophageal and gastrointestinal injury. Previous series that have included predominantly children under the age of two years have found a greater degree of drowsiness/lethargy and airway injury, in addition to esophageal and gastric injury.[1] Adult injury patterns will likely be different. Optimal management of adult patients who have ingested laundry pods is still being investigated, but evaluation with an EGD should be strongly considered.

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309. A case of death associated with ingestion of liquid neutral detergent

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Objective: To report on the autopsy case of a death associated with ingestion of neutral detergent liquid.
Introduction: Surface-active agents containing both hydrophilic and hydrophobic groups are roughly classified into cationic, anionic, and non-ionic types. Surfactants are widely used in antiseptics and cleaning products and as spreaders and emulsifiers in pesticides and in industry. These many compounds have been generally considered to be of low toxicity and to produce few serious effects except in the case of cationic surfactants, but serious symptoms and deaths associated with the ingestion of detergents have been reported.
Case report: The deceased was an 88-year-old woman who was found dead in a dining room. There was a container of liquid neutral detergent on the table. The bottle of liquid neutral detergent contained a surface-active agent (40 w/w%). Approximately, two-thirds (200 mL) of the neutral detergent remained in the bottle. She had no other clinical history except for renal dysfunction. A forensic autopsy was performed about 24h after her death. The mouth contained a large amount of white mucoid matter with foam. Autopsy revealed that the left and right lungs weighed 550 and 600 g. The lungs were congested and edematous. The duodenum also contained mucoid matter with abundant froth. Histological examination revealed corrosive changes in the bronchi. Corrosive changes were diffusely present on the mucosal surfaces of the bronchi. Toxicological investigations detected polyethylene glycol in the bronchus, blood, and gastric contents using headspace-gas chromatography/mass spectrometry.
Discussion: The action of the surfactant against protein of the cell membrane is solubilization and degeneration. When surfactants interact with the cell membrane, the surfactants introduce the membrane lipid or membrane protein into the micelles and destroy the cell membrane. This action is the cause of toxic manifestations. Although anionic surfactants have been thought to have low toxicity, several cases of serious symptoms and even death associated with the ingestion of detergent have been reported.
Conclusion: Surfactants generally have low toxicity but can cause damage to the mucous membrane of the respiratory tract. We report an autopsy case of death due to accidental ingestion of a liquid neutral detergent with special regard to the histochemical findings.

310. Severe gastric necrosis following household bleach ingestion

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Objective: Household bleach ingestions (sodium hypochlorite, concentration $< 6\%$) are typically considered to be benign, resulting in mucosal edema without significant gastrointestinal necrosis. We describe a case of severe gastric necrosis in the setting of household bleach ingestion and in the absence of ingestion of other caustics.
Case report: A 24-year-old female was brought to our emergency department after she reported ingesting 240 mL of household bleach in a suicide attempt 1 hour prior to arrival. She admitted to smoking phencyclidine as well but denied other ingestions. She had called emergency medical services due to several episodes of vomiting, the last episode of which resulted in approximately 20 mL of blood. Upon arrival the patient's vital signs were the following: temperature 37.0°C, blood pressure 120/72, heart rate 123, respiratory rate 23, with a pulse oximetry reading of 100% on room air. The patient was alert and able to answer questions appropriately. Her oropharynx was normal to inspection and her abdomen was soft with moderate epigastric tenderness to palpation. Placement of a nasogastric tube resulted in the return of blood-streaked gastric contents. An intravenous pantoprazole bolus and infusion was initiated, and a gastroenterologist was consulted. Approximately 1 hour after arrival, the patient became acutely agitated and endotracheal intubation was performed for airway protection. The patient subsequently underwent esophagogastroduodenoscopy that revealed mild erythematous mucosa in the esophagus consistent with Grade 1 esophageal injury and severe gastric necrosis.
Conclusion: Household bleach ingestions classically do not cause severe symptoms, even when ingestion is intentional. Significant caustic gastrointestinal injury is typically only reported following ingestion of higher concentrations of sodium hypochlorite, and in those cases, gastric necrosis is often accompanied by significant caustic esophageal injury.

311. Assessment of life-threatening sulfuric acid ingestion using computed tomography imaging

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Background: Computed tomography (CT) imaging is being recognized increasingly as an alternative to endoscopy in patients who have ingested corrosive agents,[1] particularly if endoscopy is considered inappropriate. However, it has been suggested that CT can underestimate the severity of injury compared to endoscopy.[2]
Objective: To describe a patient with life-threatening sulfuric acid ingestion in whom CT imaging with contrast prompted immediate life-saving surgical intervention after endoscopy was not considered safe.
Case report: A 42-year-old woman presented with hematemesis and cardiac arrest following ingestion of an unknown quantity of 91% sulfuric acid. She required aggressive intensive resuscitation with mechanical ventilation, inotropic support, correction of a metabolic acidosis (pH 7.16), analgesia, and sedation. CT abdomen was performed with contrast which identified apparent loss of the stomach and a large amount of free fluid in the abdominal cavity. Emergency laparotomy revealed a totally necrosed perforated stomach, necrotic spleen, and corrosive burns of the anterior abdominal wall and left hemidiaphragm. Total gastrectomy and splenectomy were performed with placement of a feeding jejunostomy. Ear, nose and

throat (ENT) assessment confirmed severe scarring of the pharynx, vocal cords, and epiglottis. Ocular burns resulted in partial loss of vision in the left eye and complete visual loss in the right. The immediate postoperative course was complicated by chest and abdominal sepsis and transient acute kidney injury. One year after ingestion the patient continues in rehabilitation with tracheostomy in situ and further reconstruction planned.

Conclusion: CT imaging can be valuable in the assessment of patients who have ingested concentrated acids, particularly when endoscopy is not possible.

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312. Plain abdominal radiography: A powerful tool to prognosticate zinc phosphide-poisoned patients' outcome

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Objective: Zinc phosphide is a highly effective rodenticide widely used to protect grain in stores.[1] Although not as fast as the fumigant aluminum phosphide, it liberates phosphine; thus, complications may appear later.[2] Zinc is a radio-opaque metal whose contribution may have a role in visualization of this toxic material. We aimed to evaluate the clinical features of zinc phosphide poisoning in a group of patients admitted to our center and see whether we could prognosticate their outcome based on abdominal radiography on presentation.

Methods: All zinc phosphide-poisoned patients referred to our center between March 2011 and September 2013 were retrospectively reviewed. A self-made questionnaire containing patients' demographic characteristics (age, gender), characteristics of the poisoning (amount of the toxin ingested, time elapsed between ingestion and hospital presentation, signs and symptoms on presentation, vital signs, arterial blood gas analysis, and laboratory tests), abdominal radiography results, and patients' outcome were recorded.

Results: Of a total of 163 zinc phosphide-poisoned patients referred to us, 60 were excluded because they had no abdominal radiography. Of the remaining 103, 63 were male. Mean age of the patients was 29.8 ± 11.2 years. Mean amount of ingested zinc phosphide powder was 63 grams. The most common presenting sign/symptom was nausea and vomiting in almost 60% of the patients.

Of 19 patients with problematic X-rays, 4 died, 10 developed acidosis or increased aspartate transaminase (AST) or prothrombin time (PT) and one developed renal failure ($P = 0.000$). Plain abdominal radiography had sensitivity and specificity of 64% and 88% in predicting the patients' death or development of complications. The positive and negative predictive values were reported to be 47% and 94%, respectively.

Conclusion: Plain abdominal radiography is a very good tool in prognostication of zinc phosphide-poisoned patients' outcome. A negative abdominal X-ray can strongly rule out death or later development of complications. The ingested amount of the toxin could not predict later deterioration of patients.

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313. Descriptive study of reported cases of intoxication by caustic household "hydrochloric acid" in Morocco

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Background: In Morocco caustic poisonings remain a serious public health problem due to the expensive diagnostic protocol, extended hospitalization, and possible permanent disability.[1] Hydrochloric acid is used by Moroccan households as a descaling agent, toilet bowel cleaner, and tile whitener. It is easily accessible and sold at a derisory price. It is highly corrosive, can cause serious damage to the upper gastrointestinal tract and some cases have fatal outcomes.

Objective: To describe the epidemiological profile of hydrochloric acid intoxication and particularly the circumstances of intoxication declared to the Poison Control Centre of Morocco (CAPM).

Methods: A retrospective study concerned the cases of hydrochloric acid intoxication reported to CAPM between 1980 and 2011. All cases were analyzed for demographic features, circumstances, clinical consequences, treatment undertaken, and evolution.

Results: One thousand, three hundred and sixty cases were collected; these cases accounted for 19% of all of household poisonings. The average age of our patients was 26 ± 9.45 years, range 1 to 98 years of age. Sex ratio M/F was 0.7. Adults were most commonly affected (65.8%). The most common circumstance was suicidal (45%). Accidental exposure was noted in 54%. The home remained the most common place where the poisoning occurred (94%). Patients were symptomatic in 71.1% of cases. The most frequent symptoms were gastro-esophageal (96%). The outcome was favorable in 89% of the cases. Deaths were noted in 7.1% and sequelae in 4.6%.

Conclusion: CAPM is committed to reducing the health and economic consequences due to caustic poisoning. It has taken several measures: 1. Education through awareness campaigns among the population about the risks of caustics; 2. Standardization of the management of a caustic poisoning by creating a committee of experts to develop and validate the specific action to be taken; 3. Attracting the attention of policy makers by alerts on the danger of caustic household products.

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314. A descriptive analysis of US prehospital care response to hazardous materials events

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Objective: Hazardous materials (HazMat) events involve the release of substances which could adversely affect the safety of the public. Little is known about the overall frequency and nature of these events. The few publications have involved small geographic convenience samples.[1,2,3] The purpose of the current study was to perform a descriptive analysis of events reported to a national Emergency Medical Services (EMS) database.
Methods: Analysis of the 2012 National Emergency Medical Services Information System (NEMSIS) research data set.
Results: A total of 19,831,189 events were reported, of which 2527 (1.34%) events involved HazMat response. A mass casualty incident occurred in 5.6% of events. The most common level of prehospital care was basic life support (51.1%); 2.1% required aggressive advanced life support response. The most common locations for HazMat events were homes (36.2%), streets or highways (26.3%), and health care facilities (11.6%). Industrial locations accounted for 5.4% of events. The primary symptoms observed by EMS personnel were pain (29.6%), breathing problems (12.2%), and change in responsiveness (9.6%). The most common interventions were intravenous access (19.1%), spinal immobilization (12.5%), and cardiac monitoring (11.4%). The most common medications provided were oxygen (44.5%), normal saline (12.2%), and fentanyl (1.5%). Two per cent of patients suffered cardiac arrest, with 21.7% occurring after EMS arrival; 82.6% of the patients were transported to hospitals. Median scene time was 35.5 minutes, compared with a data set median of 15.7 minutes for all calls. Barriers to patient care due to the HazMat event included response delay (21.0%), scene delay (68.1%), and transport delay (17.8%).
Conclusion: Hazardous materials events are rare causes of EMS activation in the United States. The majority occur in non-industrial venues and involve 2 or fewer patients. Scene time is frequently delayed due to multiple barriers. Cardiac arrest is rare, but occurred after EMS arrival in one-fifth of the patients.

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315. Prognostic factors in acute organophosphate poisoning

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Background: Organophosphate poisoning has a high mortality, but there is no definitive guideline for determining the severity of the poisoning and the predictive factor. The aim of this study is to investigate the prognostic factors affecting survival in patients with organophosphate poisoning.
Methods: This study included 92 patients with organophosphate poisoning from January 2005 to August 2013. We divided these patients into two groups (survivors vs. non-survivors), compared clinical characteristics, and analyzed the predictors of survival.
Results: The mean age of the included patients was 56 years (range, 16–88). The patients included 57 (62%) men and 35 (38%) women. When we compared the clinical characteristics between survivor (n = 81, 88%) and non-survivor groups (n = 11, 12%), there were no differences in renal function, pancreatic enzyme, and red blood cell and serum cholinesterase levels. However, patients who died needed more ventilatory care and experienced infections such as pneumonia and urinary tract infection more frequently than survivors. Patients who died (12) had acidemia on admission (7) and 5 had mixed acidosis and metabolic acidosis, respectively. In multiple logistic regression analysis, bicarbonate was shown to be an important prognostic factor in prediction of survival in patients with organophosphate poisoning.
Conclusion: Serum bicarbonate was the important prognostic factor and acid–base status can be helpful to predict the prognosis in organophosphate poisoning.

316. Thrombopenia and anaemia following acute 2,4-D human poisoning

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Objective: To describe unusual haematological toxicity following suicidal ingestion of 2,4-dichlorophenoxyacetic acid (2,4-D), a chlorophenoxy herbicide, which exhibits toxicity resulting from dose-dependent cell membrane damage, uncoupling of oxidative phosphorylation and disruption of acetyl-coenzyme A metabolism. Acute complications include gastrointestinal toxicity due to severe mucosal irritation, haemodynamic failure due to gastrointestinal fluid loss, vasodilatation or myocardial toxicity, and neurological disorders with coma that usually lead to death.
Case report: A 53-year-old woman with major mood disorders voluntarily ingested a glass of an aqueous solution of 2,4-D (480 g/L). She experienced vomiting soon after the ingestion and gradually developed an unconscious state that progressed to deep coma requiring intubation 2.5 hours post-ingestion. Subsequently, she experienced cardiogenic shock with left ventricular ejection fraction (LVEF) at 40% despite epinephrine and norepinephrine infusion. As lactic acidosis (pH 7.02 and lactate level > 15 mmol/L) was diagnosed, continuous veno-venous haemodiafiltration (CVVHD) and bicarbonate infusion were performed. On the next day (D1), gastroscopy evidenced exudative and erythematous esophagitis and widespread gastritis with numerous punctiform erosions and small dark necrotic areas. Proton pump inhibitors were administered, and CVVHD was anticoagulated with citrate to prevent gastric haemorrhage. On D2, blood cell count evidenced thrombopenia (79 G/L) and normocytic anaemia (haemoglobin = 10.4 g/dL) that worsened until D4-D5 with haemoglobin = 8.5 g/dL, platelets = 20 G/L, normal white cell count and no signs of disseminated intravascular coagulation. Haematological param-

eters spontaneously normalized at D8. Bone marrow examination performed at D5 was indicative of possible toxic central bicytopenia. CVVHD and inotropic drugs were discontinued on D4, and the patient was extubated on D7 after very slow consciousness recovery. She was discharged without any sequelae on D17.
Conclusion: Only 3 previously published cases described thrombocytopenia following acute poisoning with a chlorophenoxy herbicide (mainly 2-methyl-4-chlorophenoxypropionic acid/MCPP). In the 2 survivors, the decrease in platelet count was attributed to cell breakdown because it developed shortly after ingestion and rapidly normalized.

317. Epidemiology of pesticide exposures in Slovakia: A 20-year review

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Objectives: The National Toxicological Information Centre (NTIC) in Bratislava, which serves the total Slovak population of approximately 5.4 million inhabitants, has frequently been consulted for advice on pesticide exposures. To obtain more information about trends in pesticide poisonings in Slovakia, we performed a retrospective analysis of all telephone calls to the center.
Methods: Data from the NTIC database involving pesticide exposures have been evaluated for the period 1993–2012. Acute exposures were analysed for age, sex, intent of exposure (accidental or suicidal), substances ingested, and clinical severity. All intoxications were classified in accordance with the Poisoning Severity Score.
Results: During the 20-year period, 41,762 acute intoxications were reported to the NTIC, of which 4,303 (10.3%) involved pesticides. The total number of calls to the NTIC continuously increased, but the proportion of the calls concerning pesticides slowly decreased from the 13.2% in 1993 to 6.7% in 2012. Pesticide exposures in males (58.6%) were more prevalent than those involving females (33.3%). Accidental poisonings were more common (83.5%) than suicidal poisonings (13.7%). Almost half of the cases (46.0%) were children. Most exposures were caused by insecticides (44.1%), but rodenticides (24.1%), herbicides (11.4%), fungicides (8.7%), and other pesticides were also involved. Referring to the insecticides, 37.3% were organophosphates, 36.2% pyrethroids, and 8.6% carbamates. The majority of patients developed only mild toxicity (51.5%), moderate symptoms occurred in 10.1% and severe symptoms in 3.3% of all poisonings. Thirty cases (0.7%) resulted in death.
Conclusion: The number of calls to the Slovak NTIC due to pesticides in the past two decades is relatively stable. Pesticide poisonings are still associated with many fatalities, especially among patients with organophosphate exposures.

318. Burns on civilians by exposure to old WW1 chemical weapons

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Objective: The use of chemical weapons appeared in the First World War (WW1). Chlorine, mustard, and phosphorus were mainly used till 1915 (Ypres) on battlefields in France and Belgium. We report 4 cases of burns due to phosphorus and mustard exposure in civilians.
Case series: Case report 1: A 13-year-old boy presented with severe burns on his thigh. He found in a stream a white-blue colored rock, 5 cm diameter, and put it in his trouser pocket. A few minutes later it spontaneously self-ignited, and a deep 15-cm-diameter crater with punctiform burns was observed on his right thigh. Blood levels of phosphorus were insignificant. Multiple surgical care and skin grafting were needed for more than 1 year of treatment, with functional and esthetic sequelae. That day was sunny, the temperature outside was 28°C. Phosphorus ignites spontaneously at 30°C. Case report 2: A boy of 15 years presented with 2nd degree burns on his thigh after collecting a small rock red-white (rust); environmental conditions were similar. Burns were less severe needing only local topical treatment for a month. White phosphorus was identified. Case reports 3 and 4: Two civilian collectors were contaminated near Verdun battlefield, by an oily liquid while handling an old shell. After a short delay, one had second-degree burns on hands, forearms, right buttock. The second had second-degree burns of thighs, knees, and face. Together, they used a handkerchief to clean the shell and one put it in the back pocket of his trousers. Mustard gas was identified. Treatment at a burns center was required for six weeks.
Discussion: The use of chemical weapons during WW1, with an impressive tonnage (32 M. shells), has led to about 27,000 deaths and 650,000 injuries on soldiers. Various accidents in civilians (collectors) have been reported in Champagne-Ardenne (Chemin des Dames, Argonne) and Lorraine (Verdun).
Conclusion: WW1 chemical weapons are still offensive.

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319. Rapidly fatal poisoning with an insecticide containing rotenone

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Introduction: Rotenone is a botanical pesticide derived from extracts of Derris roots, which is traditionally used as piscicide, but also as an industrial insecticide for home gardens. Its mechanism of action is potent inhibition of mitochondrial respiratory chain by uncoupling oxidative phosphorylation by blocking electron transport at complex-I. Despite its classification as mild to moderately toxic to humans (estimated LD50, 300–500 mg/kg), there is a striking variety of acute toxicity of rotenone depending on the formulation (solvents). Human fatalities with rotenone-containing insecticides have been rarely reported, and a rapid deterioration within a few hours of the ingestion has been described previously in one case.

Case report: A 49-year-old Tamil man with a history of asthma, ingested 250 mL of an insecticide containing 1.24% of rotenone (3.125 g, 52.1–62.5 mg/kg) in a suicide attempt at home. The product was not labeled as toxic. One hour later, he vomited repeatedly and emergency services were alerted. He was found unconscious with irregular respiration and was intubated. On arrival at the emergency department, he was comatose (GCS 3) with fixed and dilated pupils, and absent corneal reflexes. Physical examination revealed hemodynamic instability with hypotension (55/30 mmHg) and bradycardia (52 bpm). Significant laboratory findings were lactic acidosis (pH 6.97, lactate 17 mmol/L) and hypokalemia (2 mmol/L). Cranial computed tomography (CT) showed early cerebral edema. A single dose of activated charcoal was given. Intravenous hydration, ephedrine, repeated boli of dobutamine, and a perfusor with 90 micrograms/h norepinephine stabilized blood pressure temporarily. Atropine had a minimal effect on heart rate (58 bpm). Intravenous lipid emulsion was considered (log Pow 4.1), but there was a rapid deterioration with refractory hypotension and acute circulatory failure. The patient died 5h after ingestion of the insecticide. No autopsy was performed. Quantitative analysis of serum performed by high-resolution/accurate mass–mass spectrometry and liquid chromatography (LC-HR/AM-MS): 560 ng/mL rotenone. Other substances were excluded by gas chromatography–mass spectrometry (GC–MS) and liquid chromatography–mass spectrometry (LC–MS/MS).
Conclusion: The clinical course was characterized by early severe symptoms and a rapidly fatal evolution, compatible with inhibition of mitochondrial energy supply. Although rotenone is classified as mild to moderately toxic, physicians must be aware that suicidal ingestion of emulsified concentrates may be rapidly fatal.

320. Unintentional poisoning in the elderly: Ingestion of bar soap

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Objective: Bar soaps, a subset of anionic surfactants, with an alkaline pH (9 to 11), are considered of low toxicity. Previous reports indicate a higher vulnerability to local irritating effects of bar soaps among the elderly (> = 70 years).[1,2] The objective of this retrospective study was to evaluate the circumstances of exposures as well as the frequency and severity of symptoms after bar soap ingestion in the elderly.
Methods: Retrospective inquiry in the database of two Poison Centres (1/1996-10/2013), regarding cases of oral exposure to bar soaps in the elderly.
Results: Ninety-three patients aged 70–98 years (median, 80.5) were included. Unintentional ingestions dominated (87.94%). Underlying diseases: dementia (34), psychiatric disorder (1). One person was found in a state of neglect at home; 12 seniors were in a nursing home. Forty-five seniors were asymptomatic, 33 patients developed mild symptoms, another 14 moderate symptoms. Mild swellings of lips and/or tongue were reported in 21 cases, prolonged moderate swellings of uvula, lips and/or tongue were reported in 14 other cases. Other minor symptoms were local (burning) pain (n = 4), paraesthesia (n = 1), vomiting (n = 2), belching (n = 1), abdominal pain (n = 1). Respiratory symptoms of short duration (n = 3): stridor, cyanosis, cough (one each). Local swelling after chewing or swallowing soap developed at the earliest after 20 minutes and persisted beyond 24 hours in some cases. Treatment with antihistamines and/or steroids relieved the symptoms in 9 cases.
Conclusion: Bar soap ingestion by seniors carries a risk of severe local reactions. Half the patients developed symptoms, predominantly swellings of tongue and/or lips (38%). Cognitive impairment, particularly in the cases of dementia (37%), may increase the risk of unintentional ingestion. Chewing and intraoral retention of soap leads to prolonged contact with the mucosal membranes. Age-associated physiological changes of oral mucosa probably promote the irritant effects of the surfactants. Medical treatment with antihistamines and corticosteroids usually leads to rapid decline of symptoms. Without treatment, there may be a risk of airway obstruction.

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321. Caustic and thermal eye and skin injury in four children caused by exposure to chemicals from the heating mechanism of a self-heating chocolate drink

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Objective: The mechanism of self-heating drinks is the mixture of the contents in two separate chambers consisting of calcium oxide and water, to achieve an exothermic reaction. These cases describe an exposure caused by an explosion of such a product. Calcium oxide may cause caustic burns on eyes and skin in contact with moisture.[1] To our knowledge, similar exposures are not described in the medical literature, but an accidental intake has caused caustic injury.[1]
Case report: Four 9-year-old boys were exposed to the contents of a self-heating chocolate drink. A metal ring, which was supposed to open the outer chamber, had fallen off. The boys tried to open the chamber with a wooden stick, by which they also tapped the can. The strokes initiated the chemical heating mechanism of the inner chamber, when the outer chamber was still locked. The can exploded, and the four boys were exposed to calcium oxide from the inner chamber. At the local casualty department, irrigation was initiated. On admission to the hospital, initial examination revealed considerable pain and corneal injury as well as skin burns. In three patients, some of the calcium oxide was stacked in the injured tissue in the eyes and on mucous membranes in the mouth and nose. The irrigation continued. One of the patients went home the same day. The other three stayed at the hospital for 5–9 days. Further clinical findings were injection of cornea and conjunctiva, opaque cornea, ulcers of cornea and conjunctiva and vision disturbances. Because of sequelae such as scarring of cornea and vision disturbances, follow-up examinations were required for months.
Conclusion: The chemical content of a self-heating drink gave rise to caustic and thermal injury to the eyes and skin of three children,

followed by sequelae. Poison information centers should be aware of these potential serious exposures.

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322. Role of magnesium sulphate in management of organophosphate poisoning

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Objective: To study the effects of magnesium sulphate ($MgSO_4$) on mortality and morbidity in organophosphate (OP) poisoning.
Methods: This prospective, randomized, open-label case–control study included 47 cases admitted to the emergency department of a tertiary care hospital in North India from July 2012 to October 2013. All patients with OP poisoning presenting with signs of muscarinic or nicotinic involvement were eligible for recruitment. Patients with a doubtful history of OP poisoning or with poisoning other than OP poisoning were excluded. All the patients received standard treatment including atropine, benzodiazepines for seizures, and ventilation if needed. Pralidoxime was not used. The study population was divided into two groups. Group A received $MgSO_4$ at a dose of 4 g/day in four divided doses of 1 g intravenously (IV) every 6 hours on the first day. Group B received $MgSO_4$ at a dose of 4 g/day in four divided doses of 1 g IV every 6 hours throughout the hospital stay. The primary outcome was in-hospital mortality.
Results: Forty-seven OP-poisoned patients (53% females and 47% males) were admitted during the study period. Poisoning was suicidal (90%) and accidental (10%). Baseline parameters in both groups were comparable. Group A (22 patients), treated with $MgSO_4$ for the first 24 hours of hospital stay, had a mortality of 9% (2 out of 22) and group B, treated with $MgSO_4$ through the entire stay, had a mortality rate of 20% (5 out of 25)($p = 0.164$). Patients in Group B had an increased duration of hospital stay ($p = 0.423$), duration of mechanical ventilation ($p = 0.379$), and nosocomial complications ($p = 0.008$). The mortality in group B could be attributed to nosocomial complications but $MgSO_4$ toxicity could not be ruled out. The mortality in Group A was comparable with the cohort of 70 historic controls (8.8%) treated without pralidoxime in our center.
Conclusion: Extended $MgSO_4$ supplementation in patients with OP poisoning results in increased mortality and morbidity. Magnesium supplementation (dose: 4 g/day) was not associated with any mortality benefit in OP poisoning.

323. A characterization of the overuse of toxic alcohol screening tests

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Objective: Review of appropriate testing for a toxic alcohol (TA) has not been previously studied. The primary objective of this study was to describe the patient population for whom TA testing was ordered and to determine whether appropriate utilization of testing occurred at a tertiary health system. The second objective was to ascertain if the involvement of a medical toxicologist influenced such ordering practices.
Methods: All admitted patients who had a TA, defined as methanol or ethylene glycol in this study, ordered between May 2011 and April 2013 were identified at a tertiary care center. Each chart was reviewed by two trained study investigators. Discrepancies were resolved by a third investigator. Demographics, presenting complaints, diagnoses, toxicology consult note recommendations, radiology imaging, and laboratory results were collected.
Results: A total of 85 patients had TA tests ordered, of which only 2 patients were positive for ethylene glycol and no patients were positive for methanol. Nearly 40% of patients had a history of alcohol abuse. A medical toxicologist was consulted on 28% of the cases, of which the toxicologist recommended TA testing less than a third of the time. Forty per cent of the notes documented a reason for ordering the TA panel, of which 65% of cases were unexplained acidosis. Sepsis was the discharge diagnosis (28% of cases) at almost twice the rate of the admission diagnosis (15%). Nearly 60% of cases had an initial serum bicarbonate (HCO_3) of less 20 meq/L, and 9% had a HCO_3 less than 10 meq/L. Twenty-two per cent of patients had an anion gap less than 12 and 42% of the population had an anion gap greater than 20. No subjects had oxalate crystals in their urine. Eighteen per cent of the population had an initial ethanol level greater than 150 mg/dL.
Conclusion: The proportion of positive TA tests in this study was low (<3%). History of alcohol abuse, admission for sepsis, and unexplained acidosis were the most common characteristics of this patient population that prompted TA testing. A medical toxicologist was rarely involved in cases with negative TA results; even when involved, a medical toxicologist infrequently recommended TA testing.

324. Causality assessment of herb-induced liver injury using Roussel Uclaf Causality Assessment Method

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Objective: Use of Chinese herbal medicine is common in Hong Kong. The aim of this study is to identify the herbs associated with liver injury, and describe the patterns of liver injury.
Methods: A total of 99 suspected herb-induced liver injury (HILI) cases referred to the Prince of Wales Hospital Poison Treatment Centre from 1 January 2011 to 30 June 2013 were retrospectively analyzed. The herbs implicated for each suspected case were recorded. The Roussel Uclaf Causality Assessment Method (RUCAM) was employed for the causality assessment.[1] The culprit herbs implicated in "highly probable" and "probable" cases were identified. The R ratio determines whether the liver injury was hepatocellular ($R > 5$), cholestatic ($R < 2$), or mixed ($R = 2 – 5$), where R ratio = [ALT/ULN]/[ALP/ULN].
Results: Two "highly probable" and 7 "probable" HILI cases were identified. Five patients used Chinese herbal medicines, and

4 patients used proprietary Chinese medicinal products. All cases involved use of multiple herbs simultaneously. Two cases involved use of Radix Bupleuri. Table 1 shows the culprit herbs, other herbs implicated, pattern of liver injury, and the possible hepatotoxic constituents causing liver injury.

Conclusion: HILI is not uncommon. Isolation of the culprit herb is often difficult because of use of multiple herbs simultaneously. Prolonged consumption of high-risk herbs warrants close monitoring of liver functions.

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325. Clinical application of therapeutic drug monitoring of frequently used antipsychotics

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Objective: Antipsychotics are a group of drugs for which the traditional dose–response theory is not applicable. Therapeutic drug monitoring (TDM) of these compounds is therefore mandatory. However, in everyday practice, monitoring of antipsychotics is still limited. A 1-year clinical study, approved by the local ethics committee, was started in September 2013 to evaluate the usefulness of monitoring frequently prescribed antipsychotics in 3 Belgian psychiatric hospitals.

Methods: Serum was collected from patients with a diagnosis of schizophrenia, schizophreniform, or bipolar disorder (Diagnostic and Statistical Manual of Mental Disorders [DSM] IV criteria). Patients had to be in "steady-state" condition (reached after 5–7 half-lives of the drug), which was translated as an unchanged dose of the antipsychotic in the last 7 days before blood withdrawal. Medication schemes were provided to the researchers. Samples were taken just prior to the morning dose of the antipsychotic (trough concentration). After a simple liquid–liquid extraction with methyl t-butyl ether, the serum samples were analyzed using a fully validated ultra-high pressure liquid chromatography-tandem mass spectrometric (UHPLC-MS/MS) method. This method is able to quantitate 16 antipsychotics and 8 major metabolites simultaneously. Serum concentrations were compared with therapeutic ranges defined by the Arbeitsgemeinschaft für Neuropsychopharmakologie und Pharmakopsychiatrie—AGNP-consensus group guidelines.[1]

Results: Thirty-three samples were collected in the period September–November 2013. The antipsychotics determined with the UHPLC-MS/MS method were amisulpride (5.5%), aripiprazole (3.6%), bromperidol (1.8%), clozapine (14.5%), haloperidol (12.7%), olanzapine (12.7%), quetiapine (20.0%), paliperidone (20.0%), pipamperone (3.5%), and risperidone (5.5%). Comparison with the therapeutic ranges of the AGNP group reveals that $\leq 50\%$ of the serum concentrations are within the proposed ranges.[1] Since quetiapine is a drug that is often taken only when needed, serum concentrations cannot be interpreted.

Conclusion: In this early stage of the study, the importance of TDM is already highlighted since serum concentrations are often found below the therapeutic range. Clinicians should be aware of these suboptimal serum concentrations. Adjustment of the dose in light of TDM data and the clinical effect is often indicated.

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326. The effect of obligatory review of emergency department physician requests for paracetamol serum level laboratory tests by a clinical toxicologist

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Objective: To evaluate the effect of a clinical toxicologist obligatory review and approval of emergency department (ED) physician requests to sample and send laboratory tests for paracetamol serum levels.

Table 1. Culprit herbs, other herbs implicated, pattern of liver injury, and the possible hepatotoxic constituents causing liver injury.

Culprit herb (English pharmaceutical name)	Chinese name	Patterns of liver injury	Possible hepatotoxic constituent
	"Highly Probable"		
Fructus Psoraleae	Bu gu zhi	Hepatocellular	Psoralen
Fructus Meliae Toosendan	Chuan lian zi	Hepatocellular	Toosendanin
	"Probable"		
Corydalis Rhizoma	Yan hu suo	Hepatocellular	Tetrahydropalmatine
Fructus Xanthii Sibirici	Cang er zi	Hepatocellular	Atractyloside and carbxyatractyloside
Fructus Psoraleae	Bu gu zhi	Hepatocellular	Psoralen
Radix et Rhizoma Rhei	Da huang	Hepatocellular	?Emodin
Radix Bupleuri	Chai hu	Hepatocellular	Saikosaponin
Cortex Moutan Radicis	Mu dan pi	Cholestastic	?Paeonol

Methods: Retrospective review and comparison of the appropriateness of laboratory tests for paracetamol serum levels 22 months before and 22 months after the implementation of the obligatory regulation of paracetamol blood tests by a clinical toxicologist. A paracetamol serum level laboratory test was considered appropriate if paracetamol overdosing was reported, suspected, or not excluded upon admission and the timing of blood collection was proper (first sample: 4 hours post ingestion or upon admission if the patient presented later than 4 hours post ingestion; repeated samples: expected delayed absorption or unknown ingestion time). The test or request was inappropriate if paracetamol exposure was excluded or blood was collected at the wrong time.
Results: During the study periods, 272 blood samples were tested for paracetamol serum levels; 158 samples (7.2 per month) before the implementation of the obligatory review of a clinical toxicologist and 114 (5.2 per month) samples after. Of all the samples, 28 (17.7%) and 12 (10.5%) were collected inappropriately before and after the implementation of the regulation, respectively. The difference between periods regarding all the inappropriate tests was not statistically significant, $p = 0.17$, Fisher's exact test. Comparing paracetamol test sampling appropriateness during evening and night shifts revealed significant differences. One hundred and two blood samples were collected and tested during the evening and night shifts before the regulation implementation, while only 71 tests were performed in those shifts after that date. Out of which, 20 (19.6%) and 5 (7%) samples, before and after the start of the regulation respectively, were inappropriately collected. The probability that a sample for paracetamol serum levels during evening and night shifts without a clinical toxicologist review was inappropriate was significantly higher compared to sampling after this review, $p < 0.00001$, Fisher's exact test.
Conclusion: Review and approval of ED physician requests for paracetamol serum level laboratory tests by a clinical toxicologist during evening and night shifts improved significantly the appropriateness of the blood sampling and testing.

327. How do emergency physicians make discharge decisions for alcohol-related patients?

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Objective: Blood alcohol levels may not necessarily be correlated to patient's appearance, although medical decision to discharge an acutely intoxicated patient from the emergency department (ED) is based on clinical evaluation. We investigated whether measured blood alcohol concentration (BAC) was routinely requested and whether the observation period in the emergency department allowed sufficient time for alcohol elimination before the patient was discharged.
Methods: A retrospective review of medical records of all emergency alcohol-related admissions over a 12-month period from January 2012 in patients older than 18 years was performed. Patients with co-morbid psychiatric illness and co-intoxication were excluded from the study. A BAC equal to 50 mg/100 mL was chosen because it is the legal limit, above which driving is prohibited.
Results: A total of 907 patients admitted for acute alcohol intoxication (F10.0) were included: 732 were male resulting in a male-to-female ratio of 2.1. Women were more likely to be admitted at night ($p < 0.005$). The mean length of stay (LOS) was 18.7 hours. Blood alcohol concentration (BAC) was taken in 893 patients. Records with higher BAC at admission involved patients aged 35–49 years (44.6%, $p < 0.005$) and were mostly men (71.5%, $p < 0.005$). No BAC was taken before discharge decision. Three hundred and thirteen patients were discharged with a measured BAC higher than 50 mg/100 mL. Such patients were younger (mean age, 34 years; $p < 0.005$) and male (67.33%; $p = 0.971$). Repeated ED attendances for acute alcohol intoxication were more likely to concern men (75.9%, $p < 0.05$) in the middle-age group (35–49 years, $p < 0.005$).
Conclusion: Emergency physicians (EP) routinely requested BAC at admission, but did not ask for alcohol kinetics, while the patient was being observed. The discharge decision was based on clinical judgement, when the patient is coherent and cooperative. Assessment period in ED did not allow sufficient time for alcohol elimination.

328. What are the drugs involved in sudden deaths?

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Objective: Toxic deaths are difficult to diagnose because of a lack of specificity. The aim of our study was to discuss the importance of positive results for post-mortem toxic substances and to underline how important it is to synthesize all ante-mortem data and post-mortem toxicological test results to increase the accuracy of the forensic physician when writing reports on cause of death.
Methods: We included deaths with a medicolegal objection to burial, in which a toxic cause was suspected in a monocentric and retrospective study during a 16-month period. Deaths with no identified toxic cause after medico-legal examination were excluded.
Results: One hundred and twenty-one patients were included, which represented 11.4% of the activity of the forensic unit. Toxicological results and autopsy reports identified two subgroups: 39 patients whose results indicated a toxic death (32.3%) and 54 violent deaths with associated positive blood toxic levels (44.6%). Twenty-eight were too diversified to be analyzed (23.1%). Among toxic deaths, the median age was 48.1 years, and the sex ratio of 0.7 ($p < 0.05$). Fifty-nine per cent had a post-mortem examination. Alcohol, meprobamate, and benzodiazepine levels were taken for all patients. 84.6% of patients had psychotropic drugs and 30% of them had cardiotropic drugs ($p < 0.05$). Associations of toxic substances most frequently observed were alcohol and psychotropic drugs (40%; $p < 0.05$), and particularly alcohol and benzodiazepines (33.3%). Among violent deaths with positive toxic levels, the median age was 42 years and the sex ratio was 2.8. 60.4% had

an autopsy. Alcohol and psychotropic drug levels were taken for all patients. 38.9% of them had psychotropic drugs in the blood. Benzodiazepines and antidepressants were found in association for 7.4% of patients. Antemortem data were available for 28.1% of patients, especially for women (58.8%) whose bodies were found at home (70.6%) ($p = 0.000$). They were in accordance with the usual medications prescribed in 73.5% of cases.

Conclusion: In order to target drug research and increase the accuracy in the cause of death, it is important to analyze ante-mortem data. Some psychotropic drugs with associated cardiac effects should be sought, and compared with ante-mortem elements. Emergency physicians, forensic physicians, toxicological experts, and pathologists need to collaborate in such situations.

329. Antipsychotic overdose QT nomogram risk assessment

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Objective: Antipsychotic drugs are frequently reported to cause QT prolongation both therapeutically and in overdose.[1] We aimed to review the potential risk of torsade de pointes in typical and atypical antipsychotic overdose by assessing the QT internal on the QT nomogram.[2]

Methods: All presentations to a large regional toxicology service between January 1987 and August 2013 were reviewed and any admission which included a single ingestion of an antipsychotic was extracted. Demographic information, details of ingestion (dose, time), electrocardiogram (ECG), and outcomes (arrhythmia) were obtained. Any ingestion less than the maximum recommended therapeutic dose was excluded. Only admissions with a readable ECG were included. The QT interval was manually measured on the most abnormal ECG and plotted on the QT nomogram.[2]

Results: From 3445 antipsychotic overdose presentations, there were 538 single agent supra-therapeutic anti-psychotic ingestions with a readable ECG: 16 amisulpride, 4 aripiprazole, 34 chlorpromazine, 18 clozapine, 10 haloperidol, 79 olanzapine, 36 pericyazine, 206 quetiapine, 41 risperidone, 80 thioridazine, and 17 trifluoperazine. There were no droperidol, fluphenazine, paliperidone, pimozide, prochlorperazine, ziprasidone, or zuclopenthixol ingestions that met inclusion criteria. There were no abnormal QT-HR pairs as per the QT nomogram in single ingestions of aripiprazole or haloperidol, but there were limited numbers. Within the amisulpride group, there were 9(56%) ECGs with a prolonged QT, chlorpromazine, 4(12%), olanzapine, 6(8%), quetiapine, 8(4%), pericyazine, 2(6%), risperidone, 5(12%), thioridazine, 20(25%), and trifluoperazine, 2(12%). There was 1 case of ventricular tachycardia in a thioridazine presentation with an abnormal QT. There was no significant relationship between dose and abnormal QT except for chlorpromazine.

Conclusion: Although cases of QT prolongation occurred with most antipsychotics, it was more clearly associated with amisulpride and thioridazine ingestions. The significance of small numbers of abnormal QTs, particularly at elevated heart rates, as with quetiapine, is unclear, and there may be underlying cardiac disease in some patients.

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330. Monitoring self-poisoned patients with non-invasive capnography in the emergency department: Interim analysis of the CAPNOTOX survey

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Introduction: The severity of drug self-poisoning patients can be difficult to assess, and approximately 5% of patients who are admitted to the emergency department (ED) are secondarily transferred to the intensive care unit (ICU). Several studies question the predictive power of the Glasgow coma scale, showing that an initial bad score does not predict the need for oro-tracheal intubation. Non-invasive capnography (end-tidal CO_2 – $EtCO_2$) can identify respiratory complications during procedural sedation in the ED[1,2] and could be useful in the monitoring of poisoned patients.

Methods: This prospective and blind study was conducted in a single ED to evaluate the predictive values of $EtCO_2$ measurements for the detection of complications in adult drug self-poisoning patients. Complications were defined by one of the following criteria: ICU admission, orotracheal intubation, oxygen desaturation requiring oxygen therapy ≥ 3 L/min, and bradypnea ≤ 10/min. Here, we report the preliminary results of this study.

Results: From 20/04/2012 to 20/02/2013, 104 patients were enrolled including 94 patients with measurable $EtCO_2$. The correlation between $EtCO_2$ and $PaCO_2$ showed an estimated bias of -2.7 mmHg and limits of agreement between -11.8 mmHg and 6.5 mmHg. Fifteen patients exhibited at least one complication. $EtCO_2 \geq 50$ mmHg predicted the occurrence of a complication with a sensitivity of 46.6% (95% confidence intervals [CI]: 22.3–72.8) and a specificity of 75.9% (95% CI: 64.8–84.6), which lead to a positive predictive value of 0.27 (95% CI: 0.19–0.38) and a negative predictive value of 0.88 (95% CI: 0.78–0.94). The area under the Receiver Operating Characteristic curve (AUC) of the highest $EtCO_2$ during the first 30 minutes of hospitalization was 0.74 [95% CI: 0.620–0.864]. Glasgow coma scale at admission was as powerful as $EtCO_2$ to detect complications (AUC: 0.76 [95% CI: 0.61–0.91]).

Conclusion: According to these preliminary results, the monitoring of $EtCO_2$ cannot adequately predict early complications in self-poisoned patients referred to the ED.

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