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Although it was with great sadness that we had to cancel the 2020 congress, which was to have been held in Tallinn, Estonia, due to the COVID-19 pandemic, the EAPCCT Board and Scientific and Meetings Committee decided to publish the abstracts as normal to acknowledge the work of the authors and reviewers.

1. Effect of ethanol coingestion in patients with central nervous system (CNS)-depressant intoxication

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Objective: Patients with drug abuse frequently coingest ethanol, however, the clinical relevance is not clear in larger cohorts. We investigated the clinical impact of ethanol coingestion in patients presenting to the Emergency Department (ED) with acute toxicity related to CNS-depressant drugs.
Methods: Secondary analysis on the Euro-DEN Plus data from the Munich centre concerning 640 eligible patients presenting with acute recreational drug toxicity from October 2014 to May 2019. We compared epidemiological and clinical characteristics and ED management of patients with lone CNS-depressant use (group 1) to patients who consumed CNS-depressants combined with ethanol (group 2). Furthermore, we subdivided the groups into patients tested positive for benzodiazepines and Z-drugs with or without ethanol (group B1 and B2) and opioids with or without ethanol (group O1 and O2). Drug analytics were performed with high performance liquid chromatography and immunoassay. Statistical testing was performed using the chi-squared test, Fisher exact test or Mann-Whitney U Test.
Results: A total of 425 patients were included (mean age 35 ± 9 years; 314 men (73.9%); group 1: 243 patients, 2: 182; group B1: 155, B2: 119; group O1: 197, O2: 137). Overall 416 patients (97.7%) required medical treatment, 1 patient died. Most common features were reduced consciousness (defined as Glasgow Coma Score (GCS) < 13, 62.6%) and agitation/aggression (28.9%). Overall 7.1% of all patients were intubated, 14.4% required treatment with naloxone and 6.1% with flumazenil. Additional sedation was necessary in 31.6% of all cases. Patients with ethanol coingestion had a lower GCS (group 1/2: 12/10; $p = 0.004$) with a higher prevalence of severely decreased level of consciousness (defined as GCS <9: 25.9%/41.8%; $p < 0.001$) and longer hospital stay (17 h/19 h; $p = 0.046$) but lower frequency of anxiety (12.3%/4.4%; $p = 0.004$), hallucinations (17.7%/2.2%; $p < 0.001$), agitation/aggression (35.8%/19.8%; $p < 0.001$) and psychosis (7.8%/2.2%; $p < 0.001$). The effect on sedation was particularly pronounced in patients with benzodiazepine and Z-drug ingestion (group B1/B2: GCS 11/9; $p = 0.017$, GCS <9 27.7%/43.7%; $p = 0.006$). Patients with opioid use showed severe agitation/aggression less frequently when consuming ethanol (group O1/O2: 34.5%/15.3%; $p < 0.001$). Urine analysis revealed that patients with ethanol coingestion less frequently consumed opiate substitutes (group 1/2: 59.3%/45.1%; $p = 0.004$), cocaine (13.6%/6.6%; $p = 0.021$) and synthetic amphetamines/cathinones (17.3%/6.6%; $p = 0.001$). Furthermore, less patients tested positive for more than 3 substances if ethanol was coingested (44.4%/28.2%; $p < 0.001$).
Conclusion: Coingestion of ethanol with CNS-depressant drugs leads to a more severe decrease in consciousness along with a longer hospital stay. In contrast, patients are less anxious, less frequently agitated/aggressive and show less hallucinations and psychosis if ethanol is coingested.

2. A watchful foretaste of Article 45 Annex VIII: things you will wish you knew before

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Objective: Annex VIII to Classification, Labelling and Packaging (CLP) Regulation will gradually take effect starting from 1 January 2021. It is expected to sweeten the notification process through the benefits of a well-designed database and improvement in product identification through the unique formula identifier (UFI), reducing overtreatment of patients. Nevertheless, there are some risks that could make the process turn sour. We aim to sketch a broad picture of the possible implications for Poison Centres.
Methods: We reviewed our concerns and open questions we stumbled upon during our discussions in the framework of EU stakeholder consultations.
Results: The number of submissions is expected to increase significantly resulting in a huge volume of data to be handled by the European Chemicals Agency (ECHA). Subsequently, this will put a huge burden on appointed bodies and/or Poison Centres that accept submissions in the form of administrative workload, IT-requirements and costs. Additionally, the sheer amount of notifications could make the searchable database, in-house or via the Poison Centre Notification (PCN)-portal, unworkable by slowing it down or by the inability to restrict the number of hits if there is no UFI available. Moreover, for the appointed bodies that receive the submissions, handling the complex International Uniform

Chemical Information Database (IUCLID) software format could be a hard nut to crack. If Poison Centres and appointed bodies are not ready to accept submissions before the deadline, this could threaten the quality of the advice given by Poison Centres. Furthermore, security requirements imposed by ECHA, more stringent than those required for the Cosmetic Products Notification Portal (CPNP), are a major concern, especially for smaller entities. Availability of the poison centre notification (PCN)-portal could be another issue as Poison Centres that will consult the data online will entirely depend on it. Until now, the Belgian PC has good experience with industry voluntarily notifying non-dangerous mixtures. The increasing complexity and burden of the PCN-portal could raise the threshold to voluntary notification, creating the need to install a parallel simplified system, especially for smaller companies submitting voluntary notifications. Notwithstanding these concerns, the harmonized format and product categorisation system as such have generally been welcomed as progress.
Conclusion: The harmonization of the notification through Annex VIII has brought some blessings but also a lot of complexity. It will be a challenge to fine tune the tools in time in order to have a system that is suitable for the purpose it has been created for.

3. Current experience of the Belgian Poison Centre with the new product notification requirements implementing Article 45

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Objective: According to Annex VIII of Article 45 of the Classification, Labelling and Packaging (CLP) Regulation the industry will have to submit product notifications via the European Chemicals Agency (ECHA). That obligation will be effective on 1 January 2021 for consumer and professional products and on 1 January 2024 for industrial products. ECHA decided to use the International Uniform Chemical Information Database (IUCLID) format for product notifications. The aim was to identify the major problems that the IUCLID format entails for appointed bodies.
Methods: We present the current experience of the Belgian Poison Centre (the appointed body for Belgium).
Results: Originally, the idea was to notify products in one XML file. This idea was abandoned in 2017, when ECHA decided to use the IUCLID format. This format was originally developed to record, store, maintain and exchange data on intrinsic and hazard properties of chemical substances (Registration, Evaluation, Authorisation and Restriction of Chemicals [REACH]), not to notify products. As a consequence future modifications in the IUCLID format due to changes in REACH may also have repercussions on product notifications. IUCLID dossiers are extremely complex to read. They contain one primary XML, which describes all other XMLs included in the dossier. Those XMLs define single entities (a substance, a mixture, a legal entity, etc.) that are interconnected with each other. Currently, different mixtures have to be declared separately by the submitter. As a result, appointed bodies will receive multiple notifications for one commercial product containing multiple components, each with a different mixture. There is currently no way to automatically merge these different mixtures into one commercial product. The IUCLID format is a dynamic format, resulting in a recurrent development cost for the appointed bodies to be able to support changes in the IUCLID format, which can also result in changes in the structure of the databases of the appointed bodies (and poison centres). The rigorous security requirements imposed by ECHA are a major concern. Additionally, the expected number of notifications will have a big impact on poison centres systems and on the way of searching for a specific product.
Conclusion: The choice of the IUCLID format to submit product notifications involves many problems. It is important to achieve a result that is acceptable to ECHA, appointed bodies and poison centres.

4. Toxin-induced hyperthermia in New York City: a 5-year epidemiologic review

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Objective: Hyperthermia is a life-threatening complication of agitated delirium, and a potential consequence of sympathomimetic, anticholinergic, or oxidative phosphorylation uncoupling xenobiotics. Failure to promptly cool a hyperthermic patient leads to morbid sequelae, including rhabdomyolysis, acute kidney injury, ischemic hepatitis (shock liver), disseminated intravascular coagulation, and possibly death. The primary objective of this study is to assess one Poison Control Center's (PCC) experience with hyperthermic patients, specifically as it relates to the use of ice or water bath treatment. Secondary objectives include characterizing mortality rate, ambient temperatures at the time of presentation, and initial laboratory abnormalities.
Methods: This is a retrospective analysis of data from a single PCC from 2014 to 2019. A structured query language search (SQL) of Toxicall© records initially identified all cases coded as "fever or hyperthermia." The inclusion criterion was a documented temperature of greater than or equal to 40 °C. Cases explained by an infectious or inflammatory process were excluded. Descriptive statistics and logistic regressions were performed with SPSS v25.
Results: In total 1373 Toxicall© charts were reviewed and 91 patients were identified as having hyperthermia. The average age was 40.7 years and 30.8% were female. The average peak measured temperature was 41.2 °C. The mortality rate was 17.6%. Benzodiazepines were used to sedate 47.3% of patients, diphenhydramine in 3.3% of patients, and haloperidol in 6.6% of patients. Suspected drug ingested was reported in 27 cases (29.6%). Of these, 12 cases (44%) were 3,4-methylenedioxymethamphetamine (MDMA) and 4 (14.8%) were cocaine. Five fatalities occurred in this group: 3 with MDMA and 2 with cocaine. Nineteen patients (20.9%) were placed in ice or an ice water bath as part of their cooling treatment; 5 died. The mean high temperature in New York City on days on which hyperthermic patients presented was 20.8°C. Average initial serum lactate, creatinine, and creatine kinase concentrations were 0.75 mmol/L, 185.6 µmol/L, and 10,075 U/L, respectively.
Conclusion: Hospitals continue to regularly report cases of hyperthermia to the PCC. Associated morbidity and mortality is high. Despite consistent recommendations, most patients are not sedated with benzodiazepines and are not cooled in ice or an ice water bath. This study was limited by its retrospective nature.

5. Is lithium exposure responsible for brain injuries with prolonged treatment or overdose? A rat investigation

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Objective: Lithium is the first-line treatment for bipolar disease, despite its limited therapeutic index. Three patterns of lithium poisoning including acute, acute-on-chronic and chronic overdoses following acute renal failure are described with different relationships between the resulting neurotoxicity intensity and serum lithium concentrations. Rare cases of syndrome of irreversible lithium-effectuated neurotoxicity (SILENT) have been reported following lithium overdose, mainly in acute-on-chronic poisonings. However, the exact mechanisms leading to the onset of SILENT and its predictive factors are still poorly understood. Our objectives were to investigate histological brain injuries following lithium overdose (according to the three different patterns) and prolonged treatment in the rat.
Methods: Sprague-Dawley rats were treated for three months with lithium versus saline added to their food to mimic prolonged treatment in humans (N = 12/group). Other rats were intoxicated using acute, chronic, and acute-on-chronic regimens to mimic the three lithium poisoning patterns in humans as previously described [1], with their respective controls (N = 16/pattern group). Rats were then euthanized; their brain extracted and fixed in paraffin and 2 µm slices obtained and colored. The neuropathological consequences of lithium exposure were investigated using optic microscopy (by counting the cortical neurons and astrocytes in the different brain regions) and specific immunohistological staining (using the neuron-specific NeuN monoclonal antibody, from Millipore™, and the glial anti-GFAP polyclonal antibody, from Dako™) and the New Dab detection kit of Ventana Medical Systems™).
Results: No significant brain lesion was identified in any lithium-exposed rat group in comparison to the corresponding controls. No significant increase in cell loss or vacuolization in the neurons and astrocytes as assessed using optical microscopy and immunohistological Neu-N and anti-GFAP staining was observed within each group between the lithium- and saline-exposed rats.
Conclusion: No significant brain injuries were observed following lithium exposure whatever the modalities of exposure. Lithium seems to be a functional toxicant. The mechanisms of SILENT onset cannot be explained by our rat poisoning model.

Reference

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6. Glucagon's effects on hemodynamics with and without beta-adrenoreceptor-blockade: a randomized, blinded, placebo-controlled clinical trial

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Objective: No controlled clinical studies have investigated the effects of the glucagon dose recommended for severe poisonings with ß-adrenoceptor- and calcium channel blockers [1]. We investigated the efficacy on hemodynamics and safety of high-dose glucagon with and without concomitant ß1-adrenoreceptor-blockade (ß-blockade) in healthy trial participants.
Methods: In a randomized, placebo-controlled, participant-blinded cross-over study, ten male participants each completed in random order five trial days (1-5) with combinations of a ß-blocker (esmolol), glucagon and saline placebos: 1: Saline + saline; 2: Esmolol + saline; 3: Esmolol + glucagon(-bolus); 4: Saline + glucagon(-bolus); 5: Saline + glucagon(-infusion). Esmolol (or matching saline placebo) was administered as a primed intravenous (IV) 1.25 mg/kg bolus followed by infusion of 0.75 mg/kg/minute from time −15 to 30 minutes. Glucagon 50 µg/kg (or matching saline placebo) was administered intravenously at baseline (time 0 minute) either as a bolus over 2 minutes (day 1, 2, 3 and 4) or as an infusion over 30 minutes (day 5). Hemodynamic endpoints were continuously recorded by an arterial line from time -20 to 60 minutes. The primary endpoint was mean change in heart rate from baseline to time 3 minutes. Secondary endpoints were changes in blood pressures, cardiac contractility and safety measures.
Results: On day 4 (i.e. without esmolol), the glucagon bolus increased heart rate 17 beats per minute (bpm) and systolic blood pressure (SBP) 8 mmHg from baseline to time 3 minutes compared to 0 bpm ($p < 0.001$) and 2 mmHg ($p = 0.048$) on the corresponding saline (i.e. placebo)-day (day 1). On days with esmolol (2 and 3), the glucagon bolus increased heart rate 13 bpm and SBP 11 mmHg compared to no effects of saline (p-values: < 0.001). The glucagon boluses also increased diastolic blood pressure significantly 6-9 mmHg to time 3 minutes. Hemodynamic effects of the glucagon boluses (day 3 and 4) were short-lived (<20 min). In comparison, glucagon infusion (day 5) gradually increased heart rate 13-14 bpm and SBP 17-19 mmHg from baseline to the 20-30 min time points. Nausea was common on days with glucagon but neither esmolol nor glucagon were associated with serious adverse reactions.
Conclusion: A large intravenously administered glucagon bolus caused rapid stimulatory effects on heart rate and blood pressure. The hemodynamic effects occurred regardless of ß-blockade and could also be achieved after 20-30 minutes with a continuous glucagon infusion.

Reference

[1] Howland MA. A18. Antidotes in depth: Glucagon. In: Hoffman RS, Lewin NA, Nelson L, et al. (editors). Goldfrank's Toxicologic Emergencies. 10th ed. New York (NY): McGraw-Hill Education, 2015:870–873.

7. The severity and mortality prediction of calcium-channel blocker poisoning in the intensive care unit

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Objective: Calcium-channel blockers (CCB) are responsible for life-threatening poisonings and even fatalities despite optimal

management in the intensive care unit (ICU). Previous studies mentioned the severity predictive value of blood glucose in verapamil and diltiazem poisonings. Our objectives were to assess severity prediction of blood glucose on both dihydropyridine (DHP) and non-dihydropyridine (nDHP) calcium-channel blockers and identify markers for mortality prediction.
Methods: A retrospective single-centre cohort study including all CCB-poisoned adults admitted to our ICU in 2007–2019. Severe cases were defined as fatality or need for temporary pacemaker, vasopressor and/or inotropic agent. We studied the ability of all pertinent markers on admission to predict severity and mortality, focusing on admission and peak (during the first 24 hours) blood glucose values. For the subgroup analysis, we determined if factors including blood glucose were able to identify patients who were not severe cases initially but developed severe poisoning later. Prognosticators were determined using multivariate analyses and the characteristics of the most accurate cut-off values for each parameter evaluated.
Results: Overall 177 patients (median age 52 years; 76 males/101 females) were included. Three patients ingested both DHP and nDHP CCBs and all died. In the rest, the mortality rate was 8.0% (14/174). The mortality did not significantly differ between DHP- and nDHP-poisoned patients [9.9% (7/71) versus 6.8% (7/103), $p = 0.5$]. Based on a multivariate logistic regression analysis, initial blood lactate was the only independent predictor of mortality ($p = 0.03$). Initial blood glucose was not significantly related to mortality. The optimal cut-value of lactate was 7.0 mmol/L (sensitivity, 84.6%; specificity: 83.4%). About 76.4% of the patients (133/174) met the definition of severity. The multivariate logistic regression showed that initial serum glucose ($p = 0.01$) and initial blood lactate ($p = 0.04$) were the only two independent predictors of severity. The optimal cut-values of glucose and lactate were 9.2 mmol/L (sensitivity, 62.5%; specificity, 92.3%) and 2.76 mmol/L (sensitivity, 65.6%; specificity, 80.6%), respectively. The areas under the ROC curves were 0.80 and 0.76, respectively. Seventy-five patients were not severe cases initially but 36 patients ultimately developed severe poisoning. The area under the ROC curve for initial blood glucose of overall, DPH, and nDPH groups were 0.70, 0.71, and 0.72, respectively.
Conclusion: Initial blood lactate concentration accurately predicts CCB poisoning-related mortality. Initial blood glucose concentration is an early predictor for severity but not mortality. These predictive values could be applied not only in the nDPH-poisoned but in all CCB-poisoned patients.

8. Portal embolism in hydrogen peroxide ingestion: a case series

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Objective: Hydrogen peroxide (H_2O_2) is a chemical compound widely used in low concentrations as an antiseptic and in cleaning products. Ingestion of these substances has been demonstrated to generate large quantities of free oxygen which can embolize, mainly in portal venous system [1]. Hyperbaric oxygen therapy (HBO) has been reported as a successful treatment of gas embolism, however there are no specific guidelines to treat embolism related to H_2O_2 ingestion [1,2]. We present a study on our clinical records to determine the utility of HBO in H_2O_2 ingestion cases.
Methods: We retrospectively analysed all cases of H_2O_2 ingestion collected in the last 8 years (August 2011-August 2019), in which a computerised tomography (CT) scan has been performed in order to detect oxygen embolism. Gastric lesions were classified by the Zargar score.
Results: A total of 27 patients met our criteria, and all involved ingestion of a low concentration solution (accidental 37%, voluntary 63%). Gastric endoscopy was performed in 89% of cases, 92% of which were positive for caustic lesions in the stomach. Embolism was associated with a Zargar score of 2A or higher. CT scan detected oxygen embolism in the portal venous system in 33% of cases ($n = 9$): no correlation between accidental or voluntary ingestion and the occurrence of embolism was noted. No embolism of other body areas was clinically suspected or found at CT. HBO was performed in 4 cases (44%), while 5 (56%) underwent intensive clinical observation. In both groups, further CT scans showed a complete resolution of portal embolism.
Conclusion: Portal embolism occurs in a considerable percentage of H_2O_2 ingestion cases, thus it must be considered in the clinical management of these patients. It is interesting to note how most patients of our cohort achieved a good outcome (complete resolution of embolism and no related clinical consequences) without being treated with HBO. We suggest that CT scans should be performed in all patients with lesions confirmed at gastroscopy. HBO is not essential for the resolution of portal embolism but should be performed in severe cases to treat other vascular tissue involvement.

References

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[2] Berlot G, Rinaldi A, Moscheni M, et al. Uncommon occurrences of air embolism: description of cases and review of the literature. Case Rep Crit Care. 2018;2018:1–7.

9. Colchicine: telephone enquiries to the UK's National Poisons Information Service (NPIS) and UK trends in TOXBASE® accesses and prescribing data

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Objective: Colchicine (used in the treatment of gout, Behcet's disease and pericarditis), is considered to be highly toxic and has a narrow therapeutic index. At present, there is no licensed antidote for colchicine poisoning. We assessed the incidence of colchicine poisoning reported to the UK's National Poisons Information Service together with trends in accesses to the

colchicine TOXBASE® entry and trends in prescribing data for England and Scotland.
Methods: We performed a retrospective search of the NPIS Poisoning Information Database (UKPID) to identify calls relating to colchicine (2009 to 31 July 2019) and accesses to the TOXBASE entry for colchicine (online and App). Data for colchicine prescribing in England (2014–2019) and Scotland (2013–2016) were available.
Results: Over the study period, there were 378 calls to the NPIS, of which 202 were from hospitals, involving 170 patients. Intentional ingestions accounted for 51.2% of cases; 40.0% were therapeutic errors or accidental ingestions. Poisoning Severity Scores [1] at the time of the call were as follows: none 27.6%; minor 37.1%; moderate 21.8% and severe 8.2%; (not applicable/unknown 5.3%). Outcome was known for 46/170 (27%) patients. There were 19 (11.2%) fatalities; 19 (11.2%) patients made a full recovery; 8 patients (4.7%) had ongoing features. All 19 deaths followed intentional overdoses; with a median dose of 0.36 mg/kg (range 0.19-0.79 mg/kg; 70 kg bodyweight). Call numbers from hospitals increased over the study period, with a single call recorded for the financial year 2009-2010 (no deaths); rising to 47 calls in 2018-2019 (5 deaths). Accesses to TOXBASE online for colchicine increased from 201 (financial year 2009-2010) to 725 (financial year 2018-2019). An increase in TOXBASE App accesses also occurred, from 4 accesses (financial year 2015-2016) to 115 (financial year 2018-2019). Prescribing for colchicine in England increased from 410,874 (financial year 2014-2015) to 492,405 (year 2018-2019), representing a 19.8% increase in prescriptions over the 4 year period. Prescribing data for Scotland also demonstrated an increase from 30,385 (calendar year 2013) to 41,023 (2016), representing a 35% increase.
Conclusion: The number of calls to the NPIS regarding cases and severe cases is rising in association with increasing accesses to TOXBASE and increased prescribing in England and Scotland (and likely the whole of the UK). These data reinforce the need for an effective antidote for colchicine poisoning.

Reference

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

10. An analysis of cases of methaemoglobinaemia reported in telephone enquiries to the UK's National Poisons Information Service (NPIS)

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Objective: Methaemoglobinaemia (MetHb) is a potentially life-threatening complication associated with exposure to a number of drugs and chemicals. We assessed the incidence/severity of enquiries to the UK's National Poisons Information Service (NPIS) where MetHb was reported; and the frequency of use of methylthioninium chloride (MC, methylene blue) as an antidote.
Methods: A retrospective search of enquiries to the NPIS regarding MetHb for cases reported from 2014 to 2018. The causative agent involved, the MetHb concentration and the use of MC were analysed.
Results: The NPIS received 205 enquiries (involving 187 individual patients) regarding MetHb over the 5 year study period (average 41/year). The greatest proportion of calls (78; 42%) related to recreational exposure to poppers (e.g. amyl nitrite/nitrate). Pharmaceutical agents accounted for 32 cases (17%) (dapsone n = 22; zopiclone n = 3; others n = 7) while exposure to chemicals including household products accounted for 20 enquiries (11%). Other recreational drugs causing MetHb accounted for 11 cases (6%) (cocaine n = 4; spiked drink/unknown n = 4; crystal meth n = 1; benzylpiperazine n = 1; mephedrone n = 1). In 46 cases (25%), the causative agent was unknown. Poisoning Severity Scores [1] were as follows, none 21 patients (11%); minor 63 (34%); moderate 75 (40%); severe 21 (11%); and unknown: 7 (4%). Three deaths were reported, none of which were attributed to MetHb. An admission MetHb concentration was reported in 157 patients (84%). In 23 cases it was <10%; none of these patients received MC. In 72 cases, it was 10-29% and 11 of these patients (15%) received MC. MetHb of >30% was recorded in 62 patients, 37 (60%) of which received MC. Five patients with an unknown level of MetHb were also treated with MC. Of the 53 patients who received treatment with MC, 43 (81%) received a single dose, 6 (11%) received two doses and 4 patients (8%) received three or more doses.
Conclusion: MetHb was infrequently reported to the NPIS, with recreational exposures accounting for the largest proportion of enquiries. Treatment with MC was administered in 28% of patients and in 81% of these a single dose was sufficient. Although TOXBASE defines a MetHb of 30% as the threshold for treatment, MC was administered in only 60% of these cases. Further work is required to analyse poisoning severity and the correlation between MetHb concentration, administration of MC and outcome.

Reference

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

11. Hydrofluoric acid exposure: a five-year review of enquiries made to the UK National Poisons Information Service (NPIS)

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Objective: To review enquiries to the UK NPIS involving hydrofluoric acid (HF) exposures.
Methods: A retrospective review was undertaken of enquiries relating to HF exposure between 31 May 2014 and 31 May 2019.
Results: There were 215 enquiries relating to 184 exposures; 99.5% involved patients aged 16 years and over and 89.7% were male (n = 165). Most exposures occurred by skin contact alone (n = 136, 73%), but 16 exposures involved skin contact and other routes: eye (8), inhalation (7) and ingestion (1). There were a further 23 cases of inhalation alone and 9 eye contact alone. Consistent with the occupational uses of HF, most exposures occurred in the workplace (n = 156, 84.8%). The Poisoning Severity Score (PSS) [1] was known in 179 of 184 cases. Most (81%) patients developed features of toxicity, but the majority were minor (n = 130, 72.6%). Fourteen (7.8%) patients developed moderate and 1 (0.6%) severe toxicity requiring surgical debridement. There were no deaths reported. The most common features following skin exposure alone were burns (n = 46, 33.8%), predominantly involving the hands/fingers. However, pain was reported in only 16 cases (11.8%) and erythema in 13 (9.6%). Thirty (22.1%) patients exposed by skin alone were asymptomatic at the time of the enquiry. Twenty one of these had been exposed less than 24 hours earlier and 21 had received decontamination and calcium gluconate gel applied to the area prior to the enquiry. One of the 23 patients exposed following inhalation alone developed moderate symptoms: chest pain, bundle branch block, dysphonia and bronchospasm. Of the remainder, 16 had PSS of minor and five a PSS of none (1 was unknown).
Conclusion: HF exposures reported to the NPIS are uncommon; most exposures are dermal and occur in males in an occupational setting resulting in minor features. Severe clinical features are uncommon, but severe pain and urgent surgical intervention is occasionally required. Burns may be asymptomatic in the first few hours after exposure.

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12. Enquiries to the National Poisons Information Centre in Ireland from ambulance control, emergency medical dispatchers and paramedics attending poisoning incidents from 2010-2018

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Objective: Members of the public contact ambulance control via the 999/112 emergency telephone system to seek urgent medical advice. Emergency medical dispatchers triage telephone enquiries, and are gatekeepers to the subsequent provision of pre-hospital resources by paramedics who attend the scene. We characterise the pre-hospital events, circumstances and epidemiology of acute poisoning events reported to the National Poisons Information Centre (NPIC) by ambulance control, emergency medical dispatchers and paramedics attending poisoning incidents.
Methods: A retrospective review of paramedic/ambulance control enquiries to the NPIC from 2010-2018 conducted using data from the NPIC enquiry database. Data on patient demographics, poisoning circumstances, time of enquiry, agent(s), symptoms, Poison Severity Score (PSS) and treatment recommended were collated.
Results: During the study period, the NPIC received a total of 412 enquiries concerning 383 patients from ambulance control/emergency medical dispatchers/paramedics attending the scene with a gradual increase from 2010 (n = 23) to 2018 (n = 63). Patient demographics showed that 50% of calls concerned females, 47% males with 3% unknown. The majority of calls (47%, n = 182) concerned adults (20-69 years) with 39% of calls concerning children (0-9 years). Overall, unintentional poisoning accounted for 50% and intentional/deliberate poisoning occurred in 39% of cases. Most poisoning cases (49%, n = 193) involved either prescription or over-the-counter medications and 24% (n = 94) were due to household chemicals. Symptoms were reported in 39% of patients and 88% were classified as mild (PSS =1). The most frequent initial symptoms reported were nausea and vomiting (n = 57, 38%), and decreased level of consciousness (n = 52, 34%). The majority of patients (56%) required further treatment and transport to a hospital emergency department, while 33% could be monitored at home with supervision for the development of symptoms. Temporal trends showed that the majority of enquiries occurred during the hours of 19.00-20.00, and March and August were the months with the highest incidence of paramedic enquiries. A record volume of paramedic calls occurred in October 2017 and this spike corresponds with NPIC participation at an Emergency Services Day in September 2017 to increase awareness of the Poisons Centre amongst paramedics.
Conclusion: Over the study period, there was a 2.7-fold increase in enquiries to the NPIC from ambulance control, emergency medical dispatchers and paramedics attending poisoning incidents. This retrospective review offers valuable insights into the use of emergency services following acute poisoning incidents, pre-hospital management and the need for rapid transfer to hospital emergency departments.

13. Toxicoepidemiology: a retrospective study of poisoning admissions at a referral hospital in Zimbabwe

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Objective: Poisoning is an essential problem in the public health system of Zimbabwe that causes a large proportion of admissions. In view of this, the importance of management of poisoning has been stressed in recent years. The present study therefore sets out to fill in the gap in management of poisoning at Parirenyatwa General Hospital, one of Zimbabwe`s major hospitals. We describe the management of poisoning admissions at Parirenyatwa General Hospital.
Methods: A retrospective study design was used for all poisoning admissions from 1 January 2013 to 31 December 2015 using a standard preformed data collection form using ICD-10.
Results: A total of 211 case files were obtained for the study period. The male to female ratio was 1:1.2. The 20-25 years age group was mostly commonly involved in poisoning. Deliberate self-poisoning (74.4%), was the leading cause of poisoning, followed by accidental poisoning (15.6%) and homicide (2.8%). Organophosphate insecticides (43.6%) were the major toxic agents, followed by carbamates (32.7%). Other agents responsible for poisoning were pharmaceuticals (9.5%), others (8.1%) and

unknown toxins (6.2%). The main route of poisoning was oral (99.1%). The gastrointestinal decontamination methods performed were induction of emesis (19.4%), gastric lavage (71.7%) and the use of activated charcoal (8.9%). Normal saline (52.1%) was the most commonly used IV fluid, followed by Lactated Ringer's (18.0%), 5% dextrose (14.2%), half-strength dextrose in Darrow`s solution (4.7%), 50% dextrose (1.9%) and non-specific IV fluids (4.3%). The most commonly used antidote was atropine (79.2%). Among the other drugs used diazepam (11.9%) was the most common. The mean duration of hospital stay was 2.37 days (standard deviation, 2.02). The case fatality rate was 12.3%.
Conclusion: Pesticides were the leading cause of poisoning admissions, and accidental poisoning and deliberate self-poisoning were the main circumstances that led to poisoning admissions. The patients were generally poorly managed by healthcare professionals and the case fatality rate was high for poisoned patients.

14. 109 toxicological inquiries for one patient

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Objective: Inquiries to Poison Centres may occur for reasons other than poisoning. Our electronic database of callers for the population of 10 million, records the telephone number and callers are informed that we record the call. The history of extremely curious and frequent calls concerning one patient were analysed based on the suspicion of his psychiatric problems.
Case report: A 30-year-old man, treated for asthma, was the subject of the first call in 2013, during hospitalization due to a probable inhalation of a cleaning agent containing ammonia. Later we received a further 108 calls. The number increased from 15 in both 2016 and 2017 to 33 in 2018 and 45 in 2019. The severity according to the Poisoning Severity Score was classified as 0 in 46.8% cases, 1 in 35.8% (mostly headache, tremor and dyspnoea), and the symptoms were unrelated in 17.4% of calls. Inhalation exposure prevailed (61.9%), followed by ingestion (20.9%), licking/minor ingestion (5.7%), touching (5.5%), and injection (3.8%). The reported dose was harmless in 29.4%, low in 22.9%, potentially irritating in 16.6%, and unknown in 31.2% of calls. Most calls (93.3%) came from the patient himself (up to 4/day for the same agent), most frequently on Tuesdays (19.3%) and Mondays (18.3%). The hospital called 4 times, where he was admitted several times for suspected intoxication. The man worked as a bus driver until late summer 2019 and most of the agents involved in his calls concerned car technical fluids, such as glycols (23 calls) during their exchange and refilling, gases (n = 19), including gasoline at the gas station or exhaust fumes, cleaning products for the bus body/interior (n = 14), windshield fluids (n = 5) and organic solvents (n = 5). Other sources were inspired by media and Internet sources and made him feel his life was seriously threatened. Food was blamed 15 times (botulism after accidental ingestion of dog food from the can, aflatoxins from figs, or coca cola after menthol sweet going to explode in his stomach), plants 12 times (poison hemlock potentially contaminating the bus floor, toxic cactus in a hotel, or swallowing a plum seed), insects (n = 4, small fly ingested) and pharmaceuticals (n = 5, suspected salbutamol overdose). In September 2019 he announced he works in an office and takes antidepressants.
Conclusion: Toxicologists may receive frequent and bizarre calls from patients with mental health problems and recommend them to consider consulting a psychologist. Further evolution of the calls of this patient may be interesting.

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15. Syndromic monitoring based on data from French poison control centers

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Objective: To improve the early detection of toxic-related disease outbreaks, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) and the French Poison Control Centers (PCC) have launched a syndromic surveillance system (SSS) based on the PCC database.
Methods: Experts from PCCs and ANSES have defined sixty-six "clinical entities" to be monitored. Each "clinical entity" gathered clinical symptoms available in the PCC medical records to characterize a pathological health condition. Chronological data (weekly number of cases in each entity) are analyzed daily by two methods: generalized extreme studentized deviate test (ESD) and generalized additive models (GAM). PCC and the ANSES toxicologists then assess the clinical validity of the statistical signals generated by both methods.
Results: Between April 2018 and June 2019, the SSS detected 36 signals. Eight signals (22%) were validated and 26 (78%) were not (cluster of cases having nothing in common). Among validated signals, one was an outbreak of snakebites, indicating an early snakebite season. Since there was a shortage of antidote, it allowed urging health authorities to locate the remaining antidotes and provide them where needed. Four signals were related to Datura poisoning related to the ingestion of Datura with edible plants or contained in contaminated buckwheat flour packets sold all over France, one was related to food poisonings with frozen green beans possibly contaminated with Datura, and another to the exposure of several workers to plant protection products in a greenhouse. Other signals were linked to aggregates of food poisoning cases from various causes.
Conclusion: A syndromic surveillance system using the PCC database without hypothesis on exposure agent is a useful tool to detect toxic-related disease outbreaks and could be useful to detect a terrorist attack. It can be improved by a more precise definition of clinical entities and tools to assist in signal analysis, especially for large signal sizes. Nevertheless, it does not substitute for direct reporting by physicians of unusual or suspect cases of public health importance.

16. Mapping seasonality in snake envenomation: A clue to getting ready

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Objective: Snake bite results in significant mortality and morbidity in Northwest India. Non availability of effective snake antivenom may result in increased mortality. This study was undertaken to assess the seasonality of snake envenomation at a tertiary care centre in North Western India to guide us in timely stockpiling of snake antivenom.
Methods: Retrospective study was conducted at the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, examining the case files of all snake bite patients reporting to our institute. The demographic variables, details of the date, month and time of admission were recorded. Specific emphasis was given to the month of admission, duration of hospital stay and mortality. The normative data was expressed as mean and median with percentage of patients admitted during each month.
Results: Over a period of 5 years, a total of 596 patients were admitted. Of this 432 (72.5%) were males. The mean age was 30.12 ± 14.3 years. The maximum number of patients were from Punjab (n = 208, 34.9%) followed by Himachal Pradesh (n = 182, 30.5%) and Haryana (n = 109, 18.3%). Most patient were admitted during July (n = 179, 30.0%), followed by August (n = 149, 25.0%), September (n = 97, 16.3%), June (n = 71, 11.9%) and October (n = 55, 9.2%). The number of snake bite cases starts increasing gradually from the month of May and lasts until October. This period corresponds to the monsoon season which lasts from June until August every year. The mean duration of hospital stay was 6.7 ± 6.0 days. Overall 22 patients died in 5 years.
Conclusion: Snake bite season corresponds with the monsoon season in India, with maximum snake bites occurring during this period. This information will help us stockpile snake antivenom before May every year to meet the increased demand during this period.

17. Drug-induced death in the intensive care unit in France: what are the characteristics?

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Objective: Accidental and voluntary poisonings represent a frequent cause of admission to the intensive care unit (ICU) and may result in fatal outcome. Our aim was to identify the toxicants involved in the fatal poisonings occurring in the ICU in France and compare the French situation of toxic death in the ICU to that of other developing and developed countries.
Methods: We conducted a retrospective single-centre observational study including all patients admitted to a French University Hospital ICU and who died in relation to their toxic exposure during 2010-2019.
Results: One hundred eighteen patients including 55 females and 63 males aged 52 years (27) (median, interquartile interval) were included in the study. They had a past history of depression (51%), suicide attempt (32%) and neurodegenerative disease (4%). The ingestion was voluntary in a suicide attempt (69%) involving 2 (3) toxicants. On admission, the patients presented deep coma with Glasgow Coma Score 3 (6), hypotension [systolic blood pressure, 104 mmHg (41)] and lactic acidosis [arterial pH, 7.28 (0.27) and blood lactate 8.4 mmol/L (9.7)]. Their Simplified Acute Physiology Score (SAPS) II score on admission was 77 (27). The patients were treated with mechanical ventilation (93%), norepinephrine (75%), epinephrine (76%), dobutamine (47%), isoprenaline (17%), antidotes (61%), transfusions (47%), cardioversion (25%) and renal replacement therapy (42%). The main toxicants involved in the onset of fatality were psychotropic drugs (78%), cardiotoxicants (42%), analgesics (33%), ethanol (10%) and illicit drugs (9%). The complications included the onset of pre/intrahospital cardiac arrest (35%/30%), cardiovascular (93%), renal 56%), respiratory (32%), liver (34%) and hematological failure (19%) and/or hospital-acquired infections (11%). The patients died in relation to multiorgan failure (58%), refractory cardiac arrest (34%) and brain death (8%). The death followed a decision of limitation of active therapies in 48% of the cases.
Conclusion: Our findings highlight that drug-induced death in the ICU results from the decision of limitation of active therapies in almost half of patients. Pharmaceutical drugs represent the main cause of drug-induced death in the ICU, particularly psychotropic drugs. Our observations are in agreement with observations from other countries but clearly contrast with the situation in developing countries (mainly in Asia) where pesticides represent the main cause of toxic death in the ICU.

18. Impact of manufacturer initiatives and European regulations on cases of liquid laundry detergent pod exposure registered by the French Poison Control Centres

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Objective: This study aims to assess the impact of manufacturers' initiatives and of the Classification, Labelling and Packaging (CLP) Regulation (EU-No 1297/2014) on cases of exposure to liquid laundry detergent pods (LLDPs) registered by the French Poison Control Centres (PCCs). These initiatives were introduced respectively in July 2013 and June 2015, and mainly involved changes in the labelling and outer packaging of LLDPs (by the former), and the addition of an aversive agent and heightened compression resistance of the soluble film (by the latter).
Methods: We analyzed the time series for LLDP exposure cases registered by the PCCs using a Seasonal and Trend decomposition method based on locally estimated scatterplot smoothing (LOESS) (STL). We tested the statistical significance of temporal trends in the number of LLDP cases using Kendall's tau coefficient.
Results: From 1 January 2010 to 30 April 2019, the PCCs recorded 25,817 cases of LLDP exposure: 80.8% and 15.3% concerned oral and ocular exposure respectively (of which respectively 66.2% and 93.7% cases were symptomatic). After a dramatic increase in cases of LLDP exposure between 2010 and 2013, the STL analysis showed a sharp decrease from July 2013 to June 2015 ($p < 10\text{-}3$), no significant upward or downward trend from June 2015 to June 2016 ($p = 0.23$), and surprisingly, a moderate increase since June 2016 ($p = 0.01$). Trends of crude numbers of LLDP cases were similar after adjusting for the total number of PCC cases. More specifically, whereas symptomatic oral LLDP cases have tended to decrease since July 2013 ($p < 10\text{-}3$), non-symptomatic oral LLDP cases have once again begun to increase since June 2016 ($p < 10\text{-}3$), possibly as a result of the addition of

an aversive agent. In contrast, symptomatic ocular cases have statistically increased since June 2015 ($p < 10\text{-}3$). Moreover, the available LLDP sales figures reported by manufacturers showed a clear upsurge from 2011 to 2016 and seem to have continued to rise only slightly since then.
Conclusion: While there is evidence that worldwide initiatives by manufacturers and the implementation of European regulations have had a beneficial impact on the number of cases of oral LLDP exposure registered by the PCCs, the increase in cases of symptomatic ocular LLDP exposure requires further investigation.

19. Eye injuries: case reports to the BfR from 2004 to 2018

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Objective: The German Federal Institute for Risk Assessment (BfR) receives reports on poisonings with chemical substances and products. These case reports are evaluated and documented in a standardized manner according to recognized national and international criteria in clinical toxicology. The studies MAGAM I + II on eye exposure to cleaning products, carried out by PCs, have shown that hardly any severe eye symptoms are registered if consumers are exposed [1,2]. As a complement to MAGAM, BfR has examined reported cases with eye exposures, most of which came from the occupational sector.
Methods: All cases with eye exposures submitted by physicians between 2004 and 2018 were analysed. To all agents a product categorization was assigned to identify frequently involved product groups.
Results: In the years 2004 to 2018, the BfR received 65,370 case reports on workplace exposures. Of these 40,434 cases involved eye exposure. In most cases minor health problems (Poison Severity Score [PSS1]) occurred (n = 35,776). Most commonly, eye irritations such as conjunctivitis, reddening of the eye or lacrimation were registered. Moderate eye symptoms (PSS2) occurred in 2,160 cases and severe injuries (PSS3) in 64 cases. Corneal erosions and keratitis were particularly common in moderate cases. In severe cases chemical burns of eye were observed with large corneal erosions, corneal opacities or perforations. In 81 cases permanent damage occurred or was anticipated. Due to missing data in 1,636 cases the severity could not be assessed. In 795 cases no symptoms were registered. In particular, accidents involved cleaning products (n = 9,404) followed by disinfectants (n = 4,566) and building materials such as lime, mortar or cement (n = 3,184).
Conclusion: The number and rate of cases with severe eye damage are fortunately low but irreversible damage occurs occasionally. In Germany, cases of poisonings are documented by the BfR and Poison Centres. Most case reports notified to the BfR are from the occupational sector. Both data sets might be merged in a monitoring system to provide an overview and to improve risk management measures.

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20. A worrying trend: Poisonings with pharmaceuticals in young girls in Norway

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Objective: Self-inflicted poisonings in children and adolescents, especially teenage girls, is a cause of concern according to studies in Australia [1] and the UK [2]. Our objective was to investigate the trends in pharmaceutical poisonings in 5–14-year-olds to see if there is same worrying pattern in Norway.
Methods: A retrospective review using statistics from the Norwegian Patient Registry (NPR) on hospital treatments, and the number of enquiries to the Norwegian Poison Information Centre, 2009–2018. The material was limited to pharmaceuticals. To make the groups comparable, we focused on poisonings treated in somatic hospitals, and poison centre enquiries with a predicted severity of moderate or severe poisoning.
Results: From 2009 to 2018, there was an absolute increase in somatic hospital treatments of girls aged 5–14 years for poisonings with pharmaceuticals (International Classification of Diseases (ICD)-10 code T4n) from 32 in 2009 to 81 in 2018. The increase is apparent also when compared to the total annual number of treatments for this condition (0.63% in 2009 to 1.51% in 2018). For boys, the annual numbers varied between 11 and 19, with no noticeable trend throughout the period. The number of enquiries to the poison centre concerning moderate or severe poisonings with pharmaceuticals showed a similar trend, with an absolute increase of girls aged 5–14 years from 26 in 2009 to 82 in 2018. The increase occurred almost entirely in the subgroup of girls aged 10–14 years. The trend is clear also when compared to the total number of similar enquiries. A similar increase is not found in boys. About 40% of moderate/severe drug poisonings in 5-15 year old girls and boys concerned intake of paracetamol and 10% involved methylphenidate. In contrast, approximately 20% of moderate/severe pharmaceutical poisonings in all age groups involved paracetamol.
Conclusion: Increase in poisonings with pharmaceuticals in young girls seems to be a cause of concern in Norway as seen in other countries. The same trend was not seen in boys. Paracetamol was the drug most commonly involved in potentially moderate/severe poisonings.

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21. Study on e-liquids: risk of exposure and effectiveness of regulation by Tobacco Products Directive 2

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Objective: Due to the increasing popularity of e-cigarettes, poisonings by nicotine-containing e-liquids have increased in Europe in recent years. Measures to reduce the risk posed by e-liquids have been implemented in the European Tobacco Products Directive 2 (TPD2), which entered into force from 20 May 2017. The requirements include a limitation of nicotine concentration and of container size, child-resistant closure and labelling specifications. A case data collection was performed to investigate the risk of acute poisoning by e-liquids and evaluate the effectiveness of implemented measures.
Methods: The eight German poison centres, the German Society for Clinical Toxicology (GfKT) and the German Federal Institute for Risk Assessment (BfR) conducted a pilot study to establish a national monitoring of poisonings in Germany (PiMont). In one subproject the risks of acute poisoning by e-liquids and implementation of measures defined in TPD2 were reviewed by case analysis. For a subset of cases from May 2018 to February 2019 interviews were performed to investigate details of the involved products and the circumstances of exposure.
Results: Overall 851 cases with e-cigarettes/e-liquids have been collected. Ages ranged from 4 days to 83 years; 53% of the cases related to exposure of children less than 14 years. The exposures were in the majority unintentional (83%). Ingestion was the most common route of exposure (82.4%). In the subset of 167 cases with clinical information, severity of poisoning was as follows: 50.3% (n = 84) asymptomatic, 43.1% (n = 72) minor, 4.2% (n = 7) moderate, 1.2% (n = 2) severe, 1.2% and unknown (n = 2). The disorders most commonly reported were nausea, vomiting, abdominal pain and diarrhoea. In 61 cases an interview was performed. Statements lead to the assumption that not all the products bought after implementation of TPD2 conformed to the regulation. Analysis was complicated by the fact that many consumers prefer individually mixed liquids, often stored in containers which were unlabelled and inappropriate for this purpose. Products in unlabelled containers were involved in cases with accidental ingestion and in one case with severe poisoning.
Conclusion: E-liquids containing nicotine can pose a risk, particularly for small children, if they are not stored in a safe manner. Individual mixtures usually do not fulfil expedient safety aspects such as labelling or child-resistant closures and present a further risk, not covered by the current legislation.

22. Cases of human exposure identified in 2015–2018 by the Italian surveillance system of toxic exposures and poisonings

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Objective: Since the early 1980s, the Milan Poison Control Centre has implemented a surveillance and alerting system to characterize hazardous exposures, identify unexpected events, support evidence-based prevention and legislative acts and evaluate their impact [1]. The aim of the present contribution is to provide a preliminary characterization of human exposures identified by the Milan Poison Control Centre in 2015–2018.
Methods: Descriptive analyses of the case data collected according to standard procedures.
Results: In the period under study, the Milan Poison Control Centre identified 185,544 human exposures and 3,008 animal exposures. Human exposures were characterized as follows: about 46% of the cases involved children aged less than 6 years. Male and female individuals were equally distributed. About 94% of exposures occurred at home, 2% in the workplace, and 5% were due to environmental pollution. The circumstance of exposure was unintentional for about 81% of cases, mainly related to uncontrolled access to the agent (44%), therapeutic error (11%), and decanting from the original container to another (6%). Intentional exposure occurred in 16% of cases and were mainly due to suicide attempts (14%). Clinical effects possibly related to exposure were coded in 37% of cases, while at least one treatment was required for 58%. About 39% of the cases were exposed to pharmaceuticals and 59% to non-pharmaceuticals. The most common categories of agents were: cleaning substances (household) (21%), sedative/hypnotic/antipsychotic (11%), pesticides (7%), analgesics (6%) and cosmetics/personal care products (6%), antidepressants and foreign bodies, (4%). Most animal exposures involved dogs (71%) and cats (17%). The most frequently reported agents in animal cases were pesticides (70%) and fertilizers (15%).
Conclusion: PCCs are an important source of routinely collected data on human and animal hazardous exposures and poisonings. These data can be used for improving public health at the local, national, regional and global level. In Europe, guidelines should be developed and implemented to facilitate standard data collection by Poison Control Centres, their use and comparison.

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23. Review of poisoning assessment in the Emergency Department

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Objective: Acute poisoning in children is an important public health problem and represents a frequent cause of admission to emergency units [1]. Detection of this problem in the emergency room can be challenging, especially when its assessment is not standardized [2]. Our objective was to summarize the epidemiological aspects of non-lethal poisoning cases in Muratsan University Hospital Complex, Yerevan. We believe it is important to understand the most common reasons of incidents for the prevention of accidental poisonings and suicidal attempts.
Methods: We retrospectively investigated 265 medical records of patients younger than 18 years old (2012-2019) including 121 alcohol intoxication cases, 108 suicide attempts with drug abuse and 36 cases of organophosphate poisoning (OPP).
Results: Among the suicide group, 85 (78.7%) of 108 patients, 6 (16.7%) of 36 patients among the OPP group and 105 (86.8%) of 121 patients in the alcohol group were from the capital, Yerevan. The average length of stay (ALOS) in hospital differed by gender: for males in the suicide group ALOS was 2.13 days and for females 3.04 days; males in the OPP group 4.7 days, females 4.85 days; males in the alcohol group 1.18 days, females 1.37 days (Table 1).
Conclusion: In our study there was a specific age for each group of patients with poisoning: OPP was most common in preschoolers and was usually accidental; suicide attempts occurred more commonly in female adolescents who are susceptible for psychologic risks; and alcohol intoxication cases were seen in male adolescents who tended to integrate into friend groups. The hospital stay of males in the suicide group was 30% less than females.

Table 1. Comparison of different epidemiological features in 3 groups of children and adolescents admitted to hospital, 2012–2019, with attempted suicide, organophosphate poisoning, or acute ethanol poisoning.

Patients (<18 years)	Suicide attempts (n = 108)	Organophosphate poisoning (OPP) (n = 36)	Acute alcohol poisoning (n = 121)
Age (years)	15.3	6.3	13.4
Male-to-female ratio	1 : 3.7	1.57 : 1	7.1 : 1
Average length of hospital stay (days)	2.85	4.75	1.2

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24. Epidemiology and characteristics of pharmaceutical poisoning between 2011 and 2018 in a third level hospital

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Objective: Poisoning represents about 1% of Emergency Departments (ED) visits [1,2], and approximately 42.7% of poisoning cases involve medicinal products [2]. The aim of the study was to determine the characteristics and epidemiology of patients presenting to the emergency department of the Son Espases University Hospital, Palma de Mallorca for pharmaceutical poisoning.
Methods: A retrospective observational study including 2,814 patients who presented for medicinal product intoxication at the Son Espases University Hospital ED between 2011 and 2018. Categorical variables are presented as frequencies and percentages and continuous variables were included as the mean and standard deviation.
Results: A total of 1,082,711 patients arrived to the ED during the study period. Of these 11,697 (1.08%) were poisoning related, of which 2,814 (0.26%) involved medicinal products. There was a predominance of females (56% women and 44% men); the mean age was 38.06 years (STD ±18.18) in cases discharged from the ED and 42.49 years (STD ±23.42) in patients admitted in any department. Poisonings were intentional in 84.2% (74.3% suicidal and 25.7% recreational) and unintentional in 15.8%. Most patients (82.7%) were discharged from the ED with an mean admission time of 12.16 hours (STD ±24.32), the rest of patients were admitted to different departments, most common psychiatry (9%), followed by internal medicine (3.6%), and 1.3% were admitted to the intensive care unit (ICU). A single pharmaceutical was involved in 42.8% of cases. The most common pharmaceuticals involved were benzodiazepines in 1,594 patients (56.7%) followed by analgesics in 267 (9.5%), of which 231 (8.1%) were paracetamol; antipsychotics in 248 (8.8%); selective serotonin re-uptake inhibitors (SSRIs) in 238 (8.5%) and non-steroidal anti-inflammatory drugs (NSAIDs) in 232 (8.2%).
Conclusion: As in the rest of Europe, benzodiazepines are the most common pharmaceuticals involved in poisoning [2]. Paracetamol is also among the most common drugs. We found a predominance of women in those presenting with pharmaceutical poisoning, which it different from that seen in other studies which include drug poisoning and other chemical products.

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25. Mortality and patient characteristics in paracetamol overdosing: a retrospective study

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Objective: Every year paracetamol overdose causes numerous admissions worldwide. In-hospital mortality, patient characteristics and cause of death for Danish patients are unknown. The primary aim of this study was therefore to investigate in-hospital deaths in patients with paracetamol overdose. Currently approximately 50 liver transplantations occur per year in Denmark; none of these are due to liver failure caused by paracetamol poisoning.
Methods: Data from all hospital admissions in the Capital Region of Denmark between 2010 and 2017 where the patient died in hospital along with concurrent paracetamol overdose as a diagnosis code or with a blood paracetamol concentration >0.167 mmol/L was retrieved. Medical charts were reviewed manually by a physician and data was extracted based on predefined variables. Data was analysed using R version 3.5 and Microsoft Excel.
Results: A total of 116 deceased patients were included, 46% (n = 49) with paracetamol overdose as diagnosis code and 54% (n = 67) with a paracetamol concentration >0.167 mmol/L. Mean age was 66 (range 19 to 95) years and women were overrepresented (61%, n = 71). Alcohol abuse (previous or active) was seen in 54% (n = 63). Precise dosage was seldom reported due to difficulties in retrieving medical history, but 47% of cases (n = 56) were considered acute overdose (ingestion over <24 hours) and 28% (n = 33) chronic (ingestion over >24 hours). Paracetamol was implicated in 82% (n = 99) of the fatalities (primary cause of death in 42% (n = 52) and a major or minor contributor in 40% (n = 47), 20% in both). Only one patient was signed up for liver transplantation but did not receive one in time. Dialysis (haemodialysis or continuous renal replacement therapy) was performed in 53% of patients (n = 61) and 74% (n = 85) were treated with N-acetylcysteine. Time of administration of N-acetylcysteine was registered for 49% (n = 42) and only 12% (n = 10) started treatment within 10 hours of intake. The mortality rate in the Capital Region was 1.1% (70 fatalities out of a total of 6,090 admissions with paracetamol overdose).
Conclusion: Patients aged >65 years and/or those with alcohol abuse seem to be vulnerable to paracetamol overdosing, due to comorbidities. Patients were rarely candidates for liver transplantations due to these comorbidities (primarily chronic alcohol abuse). Cause of death was often multiple organ failure at which time liver transplantation was deemed too late. Fatal outcome could possibly be avoided with earlier identification of patients eligible for antidote treatment, dialysis and liver transplantation.

26. Should I stay or should I go? One year of exposure calls to the New Zealand National Poisons Centre

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Objective: The National Poisons Centre (NPC) provides a free 24/7 telephone helpline for all of New Zealand taking calls from both healthcare professionals and the public. The objective of the study was to describe the basic epidemiology of human exposure calls made to the NPC.
Methods: Call data for human patients in 2018 were extracted and analysed, with demographic and other descriptives produced for exposure patients, and the substances characterised. The WHO World Population standard was used to calculate an age-standardised rate (ASR) of calls [1].
Results: The 20,544 exposure calls corresponded to a rate of 466.6 per 100,000 population. A total of 79% of the calls were from the public, while 18% were from healthcare professionals. Half of all patients were aged 0-4 years, and half were female. The site of exposure was a residential environment in 89% of cases. A total of 74% of patients received advice to manage the exposure on site without referral for medical assessment. The rate of medical referral varied by age from a low of 10% amongst the 0-4 year old age group, to a high of 54% amongst those aged 13-19 years. The rate of medical referral also varied by exposure circumstance, from 11% for child exploratory exposures to 96% for intentional exposures. NPC clinical toxicologists were consulted in 3.4% of all exposure calls, with 72% of these consultations occurring directly with medical professionals. Clinical toxicologists were most commonly involved in unintentional and intentional exposure consultations regarding adult patients. Most exposures involved one substance, and miscellaneous household chemicals, simple analgesics, plants, and cosmetics were the most commonly encountered classes. When the caller was a healthcare professional and a single substance was involved, paracetamol, household bleach, ibuprofen, quetiapine, petrol/diesel, zopiclone, tramadol, codeine, fluoxetine, and silica gel were most commonly encountered.
Conclusion: Most exposures reported to the NPC were paediatric, involved child exploratory behaviour, and could be managed at home. NPC clinical toxicologists advised healthcare professionals in the management and treatment of complex cases as needed. The high rates of paracetamol and psychotropic medication exposures warrant investigation about maintaining appropriate access to these substances while minimising harm through education and possible restrictions in quantities dispensed. Summary data from NPC exposure calls can inform public health policy discussions.

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27. Intentional substance exposures reported to the New Zealand National Poisons Centre

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Objective: The New Zealand National Poisons Centre routinely tracks the reasons underlying all exposure calls received and classifies them as child exploratory, unintentional, intentional (self-harm), substance abuse, therapeutic error, unknown, and other reason. This study aimed to investigate the substances in intentional exposures reported to the National Poisons Centre (NPC).
Methods: Calls where the exposure was deemed intentional self-harm were extracted for the period 1 January 2018 to 30

September 2019. Demographic and other descriptives were produced for the exposure patients and compared to exposure patients with other reasons for the exposure. The substances involved in intentional exposures were characterised.
Results: There were a total of 2,372 human patients with an intentional exposure (6.2% of all patients). Most callers were healthcare professionals (61%), while 37% were from the general public. The patient was female in 65% of intentional cases, male in 28%, and unknown gender in 7%. The median age of these patients was 20 (IQR 16-29) years, compared to 3 (IQR 1-22) years in patients whose reason for the exposure was other than intentional. A total of 96% of intentional exposure patients were advised to seek medical attention, or were already receiving such care. NPC clinical toxicologists were consulted in 12% of cases, and 94% of these consultations were for healthcare professionals. A total of 71% of patients had one substance involved in the exposure (median 1; IQR 1-2), and 98% had ingested the substance. Most exposures involved medicines, with antidepressants, simple analgesics, opioids, antipsychotics, and non-steroidal anti-inflammatory drugs the most commonly encountered classes. Where the caller was a healthcare professional, and there was a single substance involved, paracetamol, quetiapine, ibuprofen, fluoxetine, tramadol, zopiclone, sertraline, codeine, venlafaxine, and household bleach were the most common specific substances. Alcohol was used as a co-ingestant in 7% of cases, with alcohol and psychotropic medications the most common combination (52% of alcohol cases). Paracetamol was the most frequent specific co-ingestant in intentional exposures involving alcohol.
Conclusion: The typical intentional exposure call to NPC is from a healthcare professional calling about a patient who is a young woman that has ingested a single medication. The high rate of intentional paracetamol exposures is a concern, and should be addressed in New Zealand medicine policy planning.

28. Epidemiological and clinical features in acute voluntary poisoning with ethanol combined with other substances in adolescents

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Objective: To assess the main epidemiological and clinical features in acute voluntary poisoning with ethanol combined with other substances in adolescents.
Methods: We analyzed medical records of all patients with acute voluntary poisoning with ethanol combined with other substances admitted in our center over a five year period taking into consideration the following criteria: age, sex, type of co-ingested substance, symptomatology, biological findings and evolution.
Results: A total of 48 adolescents with acute voluntary poisoning with ethanol combined with other substances were admitted in our center between 2014 and 2018. The peak age group represented was 15-years-old (14 cases, 29.1%) followed by 17-years-old (11 cases, 23%). There was a similar percentage for the two genders (male 56.25%, female 43.75%). Substances of abuse were the main category of substances ingested with ethanol; 28 patients (58.3%) with cannabis being the most frequently implicated (19 cases). New psychoactive substances (2 patients), cocaine (2 cases) volatile substances (3 patients) and *Datura* (1 case) were the other substances of abuse noted. Medicines, the other co-ingested category, was identified in 18 cases (37.5%) as follows: benzodiazepines (6 cases), antipsychotics (3 cases), paracetamol (3 cases), nonsteroidal anti-inflammatories (2 cases), opiates, barbiturates and antihypertensive drug (1 case for each). The combination of ethanol + cannabis + benzodiazepines was observed in 2 cases (4.2%). Regarding the symptomatology, all the patients had vomiting, 13 (29%) sleepiness and 26 (54.2%) walking and balance disorders [1]. Coma was noted in 22 adolescents (45.8%), the most implicated combination being ethanol + substances of abuse in 16 cases. Biological disturbances were identified in few cases: acidosis in 9 patients (18.8%) and hyponatremia in 7 cases (14.6%). All patients received supportive treatment and completely recovered [1], the average length of hospitalization being 1.5 days.
Conclusion: Substances of abuse represent the main category of co-ingested substances in ethanol poisoning in adolescents; of these, cannabis is the most common. Severe neurologic disturbances like coma are frequently noted in many cases with acute voluntary poisoning with ethanol combined with other substances in adolescents (about 45% in our study); the most commonly implicated combination in our study was ethanol and substances of abuse.

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29. A comparative analysis of poisoning with acute ethanol ingestion and acute ethanol with coingestants in adolescents

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Objective: To compare clinical features of acute ethanol poisoning and acute ethanol combined with other substances in adolescents.
Methods: We analyzed the medical records of all adolescents with acute poisoning with ethanol alone or in combination with other substances, during a five year period. Data collected was age, gender, environment, and severity of clinical poisoning evaluated by the presence of coma and length of hospitalization. The patients were divided in two samples: sample 1 adolescents with acute ethanol poisoning and sample 2 adolescents with acute ethanol combined with other substances. Statistical analysis was performed using GraphPad Prism 8 program applying Mann Whitney, chi-squared and binomial test.
Results: A total of 277 adolescents with acute ethanol poisoning and acute ethanol with coingestants were admitted to our center between 2014 and 2018. The characteristics of the two samples are presented in Table 1. There was no significant difference between the two samples with respect to age, gender or environment [1]. There was no significant difference between the two samples regarding the presence of coma (41.7% versus 45.8%, $p = 0.8732$) but the length of hospitalization was significantly longer in patients from sample 2 compared to sample 1 (1.5 days versus 1.09 days, $p < 0.0001$).
Conclusion: Ingestion of ethanol combined with other substances does not significantly influence the severity of clinical features of ethanol poisoning in adolescents. Although the development of severe symptoms is not influenced by coingestants, the length

Table 1. Comparison of acute ethanol poisoning and acute ethanol poisoning with coingestants in adolescents (n = 277).

Criteria	Acute ethanol poisoning (n = 229)	Acute ethanol poisoning with coingestants (n = 48)
Gender	Male: 141 patients (61.6%) Female: 88 patients (38.5%)	Male: 27 patients (56.2%) Female: 21 patients (43.8%)
Age	11-14 years: 59 patients (25.8%) 15-18 years: 170 patients 74.2%)	11-14 years: 11 patients (22.8%) 15-18 years: 37 patients (77.2%)
Environment	Urban: 172 patients (75.1%) Rural: 57 patients (24.9%)	Urban: 38 patients (79.2%) Rural: 10 patients (20.8%)
Coma	94 patients (41%)	22 patients (45.8%)
Length of hospitalisation	1.09 days	1.5 days
Coingested substances	None	Drugs of abuse: 28 patients (cannabis 19) • Medicines: 18 patients (37.5%) • Benzodiazepines 6 • Antipsychotics 3 • Paracetamol 3 • Nonsteroidal anti-inflammatory drugs 2 • Barbiturates 1 • Opiates 1 • Antihypertensive drugs 1

of hospitalization is longer in acute poisoning with ethanol and coingestants compared to poisoning with ethanol alone.

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30. Alcohol as a co-ingestant in recurrent acute poisoning in Vojvodina, Serbia

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Objective: Self-poisoning is a considerable issue in emergency medicine and its incidence is increasing [1]. About one third of patients who deliberately harm themselves by means of poisoning repeat the self-harm within 1 year of an index episode and present to the same hospital [2]. Alcohol is very often used in recurrent poisoning, not just as a sole etiological agent, but also as a concomitant [1,2]. The aim of the study was to analyze the presence of alcohol as a co-ingestant in patients who were admitted two or more times at the Emergency Center due to acute poisoning.
Methods: Data was gathered from the medical documentation of the patients who had been treated for acute poisoning at the Emergency Center of the Clinical Center of Vojvodina (providing emergency healthcare for nearly 30% of the Serbian population) during a 5-year period (2012-2016).
Results: During the observed period 4,886 admissions due to acute poisoning were registered at the Emergency Center. Recurrence was identified in 34.7%. Two admissions were recorded in 57.1%, 3 in 17.7% and 4 in 9.1% of the patients. Alcohol was the most commonly detected etiological agent (in 70.1% of all the recurrent admissions). There were 668 sole alcohol intoxication, while in 519 repetitive admissions alcohol was co-ingested with other prominent etiological agents. The most frequently detected agents were benzodiazepines, detected in the blood of 49.6% patients, followed by mood stabilisers (18.7%) and analgesics (10.4%). The most regularly used drugs in these three groups were diazepam (66.3%), carbamazepine (51.0%), and opioids (51.6%). Abuse of psychoactive substances, registered in 64.7% of the admissions, was the most common cause of recurrence.
Conclusion: Taking into account frequency and characteristics of recurrent acute poisoning in Vojvodina, as well as possible serious interactions between psychotropic drugs and coingested alcohol, addional effort should be undertaken in order to minimise the risk among susceptible groups.

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31. Adults admitted to the emergency department of a university hospital in Belgium for acute poisoning with ethanol as a co-ingestant: characteristics and direct medical costs

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Objective: The aim of this study is to assess the characteristics and direct medical costs of poisonings with ethanol as a co-ingestant in adults (aged ≥14 years) admitted to the emergency department (ED) of the Ghent University Hospital.
Methods: Data between 1 January and 31 December 2017 were analysed using medical records and hospital invoices. Cost was defined as the cost charged by the hospital to the government and the patient. Readmissions were considered as separate admissions.
Results: A cohort of 170/1,214 (14.0%) ED admissions were included, of which 15 were readmissions. Men accounted for 64.7% of admissions. Patients aged 21-40 years (65.3%) were the largest group, followed by patients aged 41-60 years (24.7%), 14-20 years (8.8%) and >60 years (1.2%). Fifty percent of the patients were admitted on Friday, Saturday or Sunday (17.1%, 17.1% and 16.5%, respectively). Co-ingested agents most frequently involved were benzodiazepines (35.5%), cannabis (25.4%), cocaine (22.5%), psychostimulants (14.8%), antidepressants (11.2%) and antipsychotics (6.5%). Changes in consciousness were observed in 22.4%, behavioural and emotional disorders in 13.5%, and nausea and vomiting in 9.4% of admissions. A laboratory analysis was carried out in 73.5%. Eighty-four percent received psychiatric care, which is much higher than the 59.6% of patients admitted to the hospital for acute poisoning with involvement of any type of agent. Patients were discharged home after having received care in the emergency department in 48.2% of the admissions. Admissions to the emergency-department-24-hours-observation unit accounted for 31.2%, and hospitalisations or admissions to the intensive care unit for 4.7% and 5.9% of the admissions, respectively. The mean and median length of hospital stay was 1.19 (SD 3.96) and 1.0 day (IQR 0.0-1.0), respectively. In admissions of acute poisoning with involvement of all types of agents, the mean and median length of hospital stay was 1.12 (SD 3.12) and 0.0 (IQR 0.0-1.0) days, respectively. The mean and median cost per admission was $1,398 (SD $3,101) and $1,251 (IQR $209-1,544), of which 96.4% was paid by the government and 3.6% by the patient. The mean and median cost for patients with any type of agent was $1,287 (SD $2,653), and $423 (IQR $154-1,472), respectively.
Conclusion: Poisoning cases with ethanol as a co-ingestant are a limited but important group often needing psychological care. The mean cost is in the same range of acute poisoning cases involving any types of agent (7.9% higher), but the median cost is almost three times higher.

32. Evaluation of the quality of current procedures in the management of ethanol overdose in the emergency department

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Objective: Ethanol overdose is the most frequent toxicological emergency in emergency departments (EDs) in Spain. Ethanol is frequently associated with other drug overdoses and contributes to the clinical picture in traumatic injuries. The plasticity and individual variability of the symptoms ranging from severe agitation to coma, and the overlapping of other toxic or traumatic injuries, leads to a high degree of diagnostic inaccuracy and lack of standardized treatment. The aim of this work is to evaluate current deficiencies in order to stablish quality criteria for the diagnosis and treatment of these cases.
Methods: Prospective observational study of ethanol overdose cases presenting at the ED of a general hospital during 2018. Analyzed variables were: age, sex, chronology, total agents involved, diagnostic tools, symptomatology, treatment and evolution. Quality endpoints to identify improvement actions are analytical confirmation of toxic agents, capture of basic vital constants, adequacy of biochemical parameters, treatment of agitation and use of antidotes.
Results: We included 422 cases (50% of total poisoning cases), 58% men and 42% women. Mean age was 37.8 years (13-85). The distribution on week days' was uneven with predominance at weekends. Toxicological analysis was performed in 78% of cases: in blood and urine samples 62%, only blood 29% and only urine 6%. Ethanol was the only agent found in 266 of the analyzed cases. In the other cases, other drugs were also detected as co-ingestants. Most cases (83%) were due to abuse and overdose, and in 13% suicidal behavior was involved. In 19% ED admission was associated with traffic accidents or other injuries. Symptoms were neurologic 86% (inebriation, agitation and coma), cardiovascular 34%, digestive 14% and respiratory 4%. Biochemical and hematological determinations: glucose and electrolytes (62%), venous blood gases (52%), blood count (59%), coagulation (49%). Vital signs: blood pressure and heart rate (86%), temperature (76%), respiratory rate (2%), and SpO_2 (72%). Treatment was mainly supportive. Gastric decontamination was used in 9 cases due to medicine co-ingestions. Antidotes (flumazenil and/or naloxone) were used in 34 cases with no guideline indication. Symptomatic treatment included fluids (86%), thiamine (14%) and gastric protectors (7%). Treatment of agitation was very variable: physical restraint (33%), benzodiazepines 59%, and neuroleptics (21%), alone or together. A third of patients (33%) were discharged with a clinical diagnosis of inebriation without analytical confirmation.
Conclusion: We have verified the absence of standardized procedures to diagnose and treat ethanol overdose at the ED. Specific improvement points were identified in both areas.

33. Recurrent pulseless polymorphic ventricular tachycardia following acetamiprid insecticide poisoning

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Objective: Acetamiprid is a neonicotinoid insecticide. We report a patient with recurrent pulseless polymorphic ventricular tachycardia (VT) following acetamiprid ingestion.
Case report: An 81-year-old male presented with decreased consciousness and although he told his family he had ingested a bottle of insecticide, no containers were found near him. He had a history of hypertension and complicated diabetes mellitus. On arrival, he was drowsy (Glasgow Coma Score 13), with blood pressure 146/61 mmHg, pulse 56 beats/minute, and $SaPO_2$ 90% (on oxygen). Physical examination showed coarse breathing sounds, lethargy, and drooling. Initial arterial blood gases were pH 7.35, $PaCO_2$ 33.3 mmHg, PaO_2 62.5 mmHg, and base excess -6.6. Soon after arrival, endotracheal intubation with mechanical ventilation was initiated due to progressive dyspnea. Chest X-ray showed no active lung lesions. Laboratory tests showed

leukocytosis 22.3 × 10^9/L, elevated C-reactive protein 1.21 mg/dL, blood urea nitrogen 48.7 mg/dL, creatinine 3.5 mg/dL, lactate dehydrogenase 607 U/L, and normal CK-MB 3.99 ng/mL and troponin-T 0.029 ng/mL. He was initially diagnosed with organophosphate poisoning, and given an infusion of atropine (0.3 mg/h) and pralidoxime (0.5 mg/h). On day 2, his blood pressure increased to 160/60 mmHg and he was given magnesium sulfate (2-4 mg/h) following amiodarone (0.5-1.0 mg/minute) because of frequent R on T ventricular premature contractions (VPC). That evening, he had pulseless polymorphic VT with return of spontaneous circulation (ROSC) after a 200 J defibrillation. Atropine and pralidoxime were stopped. Five other episodes of pulseless VT and ROSC were observed until hospital day 4. Echocardiography showed normal left ventricle ejection fraction (62%) without wall motion abnormalities. Initial cholinesterase activity was normal (5878 U/L). Urine drug screening was positive for buprofezin (an insect growth regulator) and acetamiprid, consistent with the insecticide, "Baramtan" (acetamiprid 4%, buprofezin 15%). On hospital day 21, he was discharged with a hemodialysis schedule.

Conclusion: Our patient showed recurrent pulseless VT after acetamiprid ingestion and was successfully resuscitated after 27 defibrillations and six episodes of ROSC. The estimated dose of acetamiprid was 4 g, larger than the dose reported in a patient with severe poisoning [1]. Although neonicotinoids are of relatively low toxicity, a large dose may cause severe effects such as respiratory failure or cardiac arrest [1,2].

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34. Mass phosphine poisoning on board a cargo ship

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Objective: Fumigation of grain cargoes in the ship holds with phosphide-based substances has been widely introduced into daily practice. We present a case of mass occupational phosphine poisoning in the crew of the cargo ship sailing on the Caspian Sea.

Case report: On 18 October 2018, the "Nazmehr" Iranian cargo ship transporting grain from Aktau (Kazakhstan) to Baku (Azerbaijan) via the Caspian Sea, sent a SOS signal due to mass poisoning on board. An Azerbaijan border guard patrol ship found 12 people on board with signs of severe chemical poisoning, of which four were unconscious. According to information received, before leaving the port, the grain had been fumigated using "Quickphos" tablets containing aluminum phosphide at a dose of 560 g/kg. The crew of the ship was immediately evacuated to the Azerbaijani port of Dubandi and transferred to the toxicology unit. Upon admission to the hospital, the main symptoms of acute poisoning in the victims were: headache, dizziness, tinnitus, nausea, vomiting, lethargy, drowsiness, and stupor. They also had respiratory signs with coughing, choking, and tightness in the chest. Laboratory tests showed leukocytopenia (2.98 ± 0.74 × 10^3/μL) and thrombocytopenia (142.11 ± 45.62 × 10^3/μL) in all patients. Arterial blood gas analysis showed metabolic acidosis. In two patients the ECG showed right bundle branch block abnormality, which spontaneously resolved in a few hours. The patients were diagnosed with "acute inhalation phosphine poisoning" based on clinical suspicion, symptoms and positive chemical-toxicology tests for phosphine. Phosphine has no effective antidote and supportive care with crystalloid solution was administered. Symptomatic therapy with acid-base balance correction, antiemetics, diuretics, corticosteroids and inhalation of 100% humidified oxygen were also used for the treatment of the poisoning. By 36 hours all patients were discharged without any complications. In addition there were three other crew members who died on board before the coast guard arrived. The autopsies showed that death occurred due to profound shock, acute myocarditis and multi-organ failure.

Conclusion: This mass occupational poisoning in seafarers occured due to failure in the ship safety requirements, decrepitude of the vehicle and the lack of tightness of the holds. The incident showed the necessity for a serious strengthening of control over the observance of safety rules during transportation of fumigated goods on the Caspian Sea.

35. Amitraz: an unfamiliar insecticide with familiar toxicity

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Objective: Amitraz is a pesticide used worldwide in agriculture and veterinary medicine for its insecticide and acaricide properties, respectively. While toxicity in humans is uncommon, ingestion results in a multitude of manifestations primarily due to effects on central and peripheral α_2 adrenergic receptors, as well as inhibition of monoamine oxidase (MAO) enzyme activity and prostaglandin E_2 synthesis. We report a case of intentional amitraz ingestion to emphasize clinical treatment strategies.

Case report: A 27-year-old male cattle farmer presented to a rural Kenyan Emergency Department (ED) after reported intentional ingestion of a 20 mL bottle of a pesticide whose active ingredient was amitraz 12.5% 4 hours prior to arrival. Initially, he was unresponsive and exhibited miotic pupils, a narrow complex bradycardia (heart rate of 45 bpm), hypotension (blood pressure 60/40 mmHg), hypoxia (O_2 saturation 84%), depressed respirations, and a temperature of 37.4 °C. Blood glucose was within normal limits. Supportive care including 15 L of oxygen via a non-rebreather, intravenous access, and a 2 liter bolus of normal saline were rapidly initiated. Atropine 1 mg and naloxone 6 mg were administered with no response. Repeat blood pressure was unobtainable by peripheral cuff, and central pulses were markedly reduced in amplitude. The patient received epinephrine 1 mg with improvement in hemodynamics, and he was subsequently intubated and mechanically ventilated. Dopamine infusion was initiated at 5 μg/kg/min for continued hypotension and bradycardia. The patient was admitted to the intensive care unit and was weaned off inotropic support within 12 hours. He spontaneously awoke approximately 24 hours after initial ingestion and self-extubated with full recovery allowing hospital discharge shortly thereafter.

Conclusion: Amitraz is an agricultural chemical with widespread use in rural Kenya that is often ingested in an attempt at self-harm. Its systemic manifestations are myriad but most commonly include hypotension, bradycardia, miosis, CNS depression, and vomiting resulting from central alpha-adrenergic agonism. With no antidote, care is largely supportive including aggressive respiratory and hemodynamic support with intravenous fluids and inotropic/vasoactive agents. Naloxone has been utilized in

ingestion of other centrally acting alpha-adrenergic agents such as clonidine, but its effectiveness in amitraz ingestions has not been well delineated. Yohimbine has also been proposed as a treatment option but was deferred in this patient due to improvement with aggressive supportive care. In this case, inotropic support and mechanical ventilation were able to sustain hemodynamics until the substance was metabolized to non-lethal xenobiotics.

36. Assessment of the effectiveness of gastric lavage in organophosphorus poisoning by quantifying pesticide in lavage fluid

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Objective: There is low quality evidence on the effectiveness of gastric lavage in organophosphorus poisoning [1]. This study was done to estimate the quantitative level of chlorpyrifos and quinalphos in gastric lavage fluid and to determine whether the pesticides are present in the stomach after 1 hour of ingestion.
Methods: Patients presenting within six hours of alleged history of ingestion of quinalphos or chlorpyrifos were included in the study. All patients were given standard treatment. After stabilizing the general condition of patients and atropine administration to dry up secretions, gastric lavage was done through a nasogastric tube. Gastric contents were aspirated using 200 mL normal saline and a 10 mL sample was taken for analysis. Further aliquots of 200-300 mL of saline were given and the liquid drained by gravity or aspirated out repeatedly until the aspirate was clear. A blood sample was also taken for confirmation of exposure. Quantification of the pesticide was done with gas chromatography with triple quadruple mass spectrometry (GC-MS).
Results: A total of 12 patients were included in the study of which there were six patients in each pesticide group. There was one female in the chlorpyrifos group and all the remaining patients were male. All patients presented after one hour of ingestion and two patients after 4 hours. Mean age, time of presentation and quantity of pesticide in the lavage fluid in the chlorpyrifos group were 49.8 ± 16.4 years, 219.2 ± 119.3 minutes and 27.4 ± 41.3 (range 7.1-110.8) µg/L. For quinalphos the mean age, time of presentation and quantity of pesticide in the lavage fluid was 58.8 ± 3.3 years, 141.0 ± 50.5 minutes and 3168.7 ± 4916.6 (1.2-13058.5) µg/L. Other compounds detected in lavage fluid and confirmed in blood were endosulfan, diazinon, pirimiphos, pyridafenthion, pyrazophos, pirimiphos ethyl and azinphos.
Conclusion: Chlorpyrifos and quinalphos are present in the stomach after one hour of ingestion and detected up to 6 hours after ingestion. We also confirmed the presence of other pesticides in commercially available chlorpyrifos and quinalphos preparations, including endosulfan.

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37. Pesticide poisoning: A retrospective study of cases reported to the Poison Control and Pharmacovigilance Center of Morocco (2009–2018)

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Objective: This study aims to determine the main epidemiological characteristics of pesticide poisoning and to identify risk factors in Morocco.
Methods: This is a retrospective study of cases of pesticide poisoning reported to the Poison Control and Pharmacovigilance Center of Morocco between 2009 and 2018.
Results: During the period of study, 13,161 cases of poisoning by pesticides were registered in Morocco, nearly 1316 cases per year, on average. Adults were involved in 47.9% of cases. The average age of patients was 21.1 ± 14.5 years and the sex ratio was 1.5 with a female predominance. The occurrence of intoxication was essentially accidental in 48.9% of cases. In addition, 59% of poisonings were recorded in urban areas; and 71.7% occurred at home. The most incriminated products were rodenticides (42%), particularly, alphachloralose; followed by insecticides (39.7%), of which organophosphates were involved in 43.6% of cases. The most common route of intoxication was oral (83%). Overall, 37.6% of cases were classified as grade 2 using the Poison Severity Score [1]. Of the 8893 cases for which the outcome was known, 384 deaths were recorded, representing a fatality 4.3%. Death case analysis showed that it was closely related to aluminum phosphide poisoning ($p < 0.05$).
Conclusion: The extent of the problem related to pesticide intoxication could be assessed from the Poison Control and Pharmacovigilance Center database of Morocco, which is a reference for the identification of cases of intoxication and allows identification of new risks. This analysis can be used to encourage policy makers, manufacturers and regulators to take action to prevent and control this issue.

Reference

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38. Fatal molluscicide poisoning

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Objective: We report a case of occupational pesticide poisoning based on metaldehyde.
Case report: The 55-year-old patient worked on a farm, and had no notable pathological history. The history of the disease began with the appearance of redness of the face and then respiratory discomfort following handling of a pesticide for agricultural use. At admission to the emergency department, he was conscious with facial urticaria, flushing, tachycardia at 140 beats/min and difficulty breathing. The patient was hospitalized and given oxygen therapy and antihistamine treatment. Twenty-four hours later, he had nausea, vomiting, muscle cramps, motor deficit of the left lower limbs and then of all 4 limbs, abnormal movements (like tremor) and frontal syndrome with cognitive disorder; all evolving in a context of hyperthermia at 38.8 °C. The biological assessment showed renal insufficiency (urea 1.23 g/L, creatinine 26 mg/L), metabolic acidosis (pH 7.19, bicarbonate 9 mEq/L), rhabdomyolysis with creatine kinase 19366 µg/L and a slight elevation of transaminases. An infectious bioassay and chest X-ray were unremarkable, eliminating an infectious cause. Cerebral magnetic resonance imaging (MRI) showed bilateral and symmetrical temporo-parietal cortical involvement, primarily post-toxic laminar cortical necrosis. In view of this, a thorough anamnesis revealed the use of a metaldehyde in the days preceding the symptomatology and a massive and repeated occupational exposure for several months before without any means of protection. The toxicology analysis was not done by default of means. Despite attempts to correct vital functions, evolution was marked by hemodynamic status deterioration and severe acidosis resulting in death.
Conclusion: The use of pesticides in Morocco is generally not in accordance with good agricultural practice. To improve people's health and preserve the environment, action must be taken to secure the safe management of agrochemicals.

39. Glucose-insulin-potassium (GIK) infusion for the treatment of acute aluminum phosphide poisoning

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Objective: Acute aluminum phosphide poisoning is common in low- and middle-income countries, and is associated with very high mortality. The addition of glucose-insulin-potassium (GIK) infusion to standard supportive care has been found to improve outcome. We aimed to assess the effectiveness of GIK infusion in acute poisoning from aluminum phosphide.
Methods: We performed a prospective interventional study in a tertiary care hospital in north India in patients over 13 years of age with acute aluminum poisoning, to determine whether treatment with GIK infusion improved outcome. The primary outcome was in-hospital mortality, and the secondary outcomes were the duration of hospital stay, the requirement of mechanical ventilation, and the change in hemodynamic and metabolic parameters.
Results: A total of 60 patients were assigned to groups that received either GIK infusion with supportive care or supportive care alone. Baseline parameters in both groups were comparable. Treatment with GIK infusion was associated with significantly low in-hospital mortality compared with supportive care alone (46.7% versus 73.3%; *p*-value 0.03). GIK infusion was associated with longer duration of hospital stay (*p*-value <0.01) and reduced requirement of mechanical ventilation (*p*-value <0.01). The treatment improved blood pressure (systolic, diastolic and mean arterial pressure) and Glasgow Coma Score at various time intervals; however, pulse rate and metabolic acidosis (pH and bicarbonate) remained comparable in both groups. Hyperglycemia was significantly higher in GIK group.
Conclusion: Treatment with GIK infusion improves survival and hemodynamics in patients with acute aluminum phosphide poisoning.

40. The impact of obidoxime on duration of hospitalization in acute organophosphate poisoning in Muratsan University Hospital, Yerevan, Armenia, 2012–2019

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Objective: Acute organophosphate (OP) pesticide poisoning causes tens of thousands of deaths each year across the developing world. Standard treatment involves the administration of intravenous atropine and obidoxime to counter acetylcholinesterase inhibition at the synapse [1]. The aim of this study was to assess the patterns of acute organophosphate poisoning (OPP) and compare treatment regimens in Muratsan University Hospital.
Methods: We studied records of 36 nonlethal cases of OPP retrospectively among children and adolescents aged 1-18 years from 2012 to 2019.
Results: In the group of patients who received obidoxime the mean age was 12.2 years and in the non-obidoxime group mean age was 4.6 years. Among the 36 cases studied, 61.1% were male, and 38.9% were female. The time lag between poisoning and hospital admission on average was 5.5 hours (range 0.5-48 hours). The main complications were cholinergic crisis (n = 30), gastroesophagitis (n = 24), respiratory failure (n = 8), seizures (n = 4), pancreatitis (n = 4), cystitis (n = 1) and cardiovascular failure (n = 1). The haematology parameters were generally normal, except for slight inflammatory changes in few patients. Liver function tests, BUN, creatinine, calcium and sodium concentrations were in normal ranges. Three 3 subjects had hyperglycemia, 6 patients had hypokalemia, and in 5 cases serum amylase levels was increased. Diagnosis was supported by decreased levels of acetylcholinesterase. The average length of stay (LOS) in hospital was 6.3 days (range 1–13 days).
Administered therapy involved gastric lavage, repeated doses of activated charcoal, atropine and obidoxime. All 36 patients received multiple doses of atropine by IV bolus (0.02-0.05 mg/kg) as needed for 5.2 days on average (range 1–2 days). In 8 cases with clinical manifestations of nicotinic symptoms we used obidoxime (25 mg/kg by IV bolus) and rapidly repeated doses as

needed for up to 2–3 days. In the group of patients, who underwent treatment with atropine + obidoxime, the average LOS was 4.5 days, in contrast to 6.1 days in those given only atropine. Two patients required intubation for airway control and adequate oxygenation.
Conclusion: This case study concluded that addition of obidoxime to the treatment plan decreases the length of stay in hospital and increases the effectiveness of therapy in patients with OP poisoning. We therefore suggest starting therapy with obidoxime in all patients with OP poisoning, without regard to complications present.

Reference

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41. Poisoning risk of acute exposures to repellents: results from a prospective observational study

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Objective: Repellents are applied to skin, clothing or other surfaces, mainly for bite protection for the prevention of arthropod-borne infections. The most common active ingredients of topical repellents are diethyltoluamide (DEET), icaridin (picaridin), p-menthane-3,8-diol (PMD), IR3535 (ethylbutylacetylaminoproprionate) and a range of plant-derived extracts (e.g. melaleuca, eucalyptus, citronella oils). Acute toxicity of these ingredients derived from animal testing differ substantially. The aim of the study was to analyse poisoning risks caused by acute exposures to repellents.
Methods: The eight German poison centres (PCs), the German Society for Clinical Toxicology (GfKT) and the German Federal Institute for Risk Assessment (BfR) conducted a pilot study to establish a national project monitoring poisonings in Germany (PiMont). In a subproject exposures to repellents reported to PCs from May 2018 to May 2019 were prospectively collected. Product name, clinical data and circumstances of exposure were analysed.
Results: Overall 262 exposures to a single repellent product were recorded (224 children, 38 adults). Accidental exposures dominated (256, 97%). Routes of exposure were oral (186, 71%), dermal (35, 13%), ocular or inhalation (26 each, 10%). More than one route of exposure was reported in 23 cases (8%). Severity of poisoning was asymptomatic (n = 183, 69.4%), minor (n = 78, 29.8%) or moderate (n = 1, 0.4%). In the latter, case symptoms were assessed as unrelated to exposure. Most ocular exposures were symptomatic (85%), whereas after inhalation only 42% and after oral ingestion 18% reported symptoms. Most common were exposures to products containing icaridin (n = 89), PMD (n = 40), DEET (n = 39), and plant extracts (n = 21). Product identification was not possible in 54 cases (21%). Overall 34% of exposures to icaridin, 26% of exposures to DEET and 30% of exposures to PMD were symptomatic.
Conclusion: Only minor symptoms or no symptoms were registered in all cases. The highest rates of symptomatic cases were recorded after ocular exposure, followed by inhalation, and ingestion. Exposures to icaridin were registered most often. The rate of symptomatic exposures was slightly higher for icaridin than for DEET. Thus, the poisoning risk of acute accidental repellent exposures seems to be low.

42. Human exposures to pesticides: results of a subproject of the German pilot study PiMont

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Objective: Compilation of poisons centre (PC) data facilitates health reporting and sensitive detection of unusual case series, but is challenging if only partially harmonized case databases are used. As a model for case data collection in Europe all eight German PCs, the German Society for Clinical Toxicology (GfKT) and the German Federal Institute for Risk Assessment have conducted a pilot study to establish national monitoring of poisonings in Germany (PiMont). In one subproject pesticide poisonings were reported, mainly to fulfil legal reporting needs (e.g. (EU) No 528/2012).
Methods: Prospective observational study from 1 May 2018 to 28 February 2019. Human exposures to pesticides reported to all PCs in Germany were included. A basic dataset (age or age-group, sex, number of patients, date of call, route of exposure, agent, circumstances) was collected for all cases.
Results: A total of 2,647 (persons affected 2,808) prospective reports on pesticides were collected. The majority of exposures (88.5%) were accidental. Children between 1 and less than 6 years were mostly involved (n = 1,111, 39.6%) with oral exposure (n = 850, 76.5%). Furthermore, products with "critical agents" were detected in 89 cases. These include plant protection products whose approval has already expired or that have been banned (e.g. parathion, banned in the EU since 2001). Nevertheless, these products are still privately owned and used for suicidal acts.
Conclusion: The PiMont pesticides dataset provides a reliable quantitative overview of pesticide poisoning events reported to PCs in Germany, facilitating legal European and national reporting obligations. Furthermore, agents that have been banned

could still be detected. Especially for parathion the ban does not apply to exports of the substance across the EU's external borders. The number of cases has decreased, but not completely disappeared [1]. Data of heterogeneous PC case databases could be collated successfully via the Web-based GfKT Case Database after quality control and used for recording within a continuous monitoring project.

Reference

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43. Organophosphate poisoning among children and adolescents in Armenia: a retrospective case study

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Objective: Organophosphate compounds are widely used pesticides. Toxic effects result from excessive cholinergic stimulation through inhibition of acetylcholinesterase [1]. The aim of this study was to assess the pattern of acute organophosphate poisoning (OPP) in Muratsan University Hospital.
Methods: Retrospective chart review of OPP among children and adolescents aged 1-18 years from 2012 to 2019.
Results: Overall 36 patients were included; most were male (F/M ratio 1:1.57). Mean age was 6.3 years (range 1-18 years). There were 6 patients (16.7%) from Yerevan and the remaining 30 (83.3%) were from surrounding provinces (Ararat n = 12, Armavir n = 10, Kotayk n = 4, Gegharkunik n = 3 and Lori n = 1). Most (35 cases) were accidental poisonings and 1 case was a failed suicide attempt. All cases were the first time the patient had been exposed to OPs. Time lag between poisoning and hospital admission on average was 5.5 hours (0.5-48 hours). Common symptoms were nausea/vomiting (n = 32), paleness (n =3 2), abdominal pain (n = 28), fatigue (n = 28), hyperhidrosis (n = 17), miosis (n = 17), alterations in consciousness (n = 14), hypersalivation (n = 14), fasciculations (n = 12), tremor (n = 12), headache and dizziness (n = 8), diarrhea (n = 7), impaired accommodation (n = 5), lacrimation (n = 5) and seizures (n = 4). Other less common signs were polyuria, dyspnea, bronchorrhea and diplopia. Hematology and erythrocytes were normal, except for leukocytosis (maximum 27.4×10^9/L) in 5 patients. Liver function tests were in normal ranges or slightly increased, 3 subjects had hyperglycemia (around 10 mmol/L), and BUN and creatinine were normal. There were 6 cases of mild hypokalemia; calcium and sodium were generally normal. Five patients had increased serum amylase. Acetylcholinesterase activity was decreased in all patients. All patients received atropine, obidoxime and diazepam and symptomatic treatment, except for two patients who required intubation and artificial ventilation. In the group that presented in less than 6 hours between poisoning and hospital admission the mean time of hospitalization was 4.34 days and in the group presenting ≥6 hours the mean hospitalization time was 6.26 days. There were no deaths.
Conclusion: The vast majority of patients (83.3%) were from neighboring provinces since the main agricultural facilities are located there. We believe that the reason of the absence of patients from farther regions is the distance from Yerevan (the capital city). There was longer hospitalization in those with delayed admission and we recommend treating patients in farther regions at the local hospital level.

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44. Lethal intoxication by pentachlorophenol

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Objective: Pentachlorophenol (PCP) is a lipid-soluble polychlorinated aromatic compound used as a pesticide or wood preservative. It is banned in many countries or rarely used because of its stability, persistence in the environment and toxicity. Indeed, occupational poisoning has been reported since 1952. We describe a case of fatal intentional intoxication.
Case report: A 64-year-old man was admitted to the emergency department (ED) with vomiting, confusion, tachycardia and tachypnea. From the history provided by his family, he was treated initially for intoxication with permethrin and coformulants. Gastric decontamination, fluids and symptomatic treatment were performed, with intensive monitoring of vital signs and metabolic parameters. One hour later it became known that he had actually ingested a large amount of PCP. Meanwhile the clinical picture had deteriorated; he has become catatonic and sweaty, with continuing tachycardia and vomiting, with metabolic acidosis. Two hours after admission he developed severe respiratory distress with cyanosis, hyperkalemia (11.8 mEq/L), hyperglycemia (750 mg/dL), hyperthermia (38.8 °C), bradycardia and finally had a cardiac arrest. The patient died a few hours after hospitalization.
Conclusion: The use of PCP is restricted compared to the past, due to its toxicity following both acute and chronic exposure. PCP is a lipid-soluble molecule that can be rapidly absorbed through the skin and the respiratory and gastrointestinal tracts. The main mechanism of toxicity has been associated with mitochondrial damage and the uncoupling of oxidative phosphorylation, that can explain some features of acute systemic poisoning such as hyperthermia, sweating and metabolic acidosis. Other symptoms are lethargy, weakness, alterations of consciousness, tachycardia, tachypnea, hyperglycemia, and intravascular hemolysis. In addition, spasms, muscle twitching, convulsions and rigor have also been described [1,2]. Management of intoxication is supportive and is aimed at controlling body temperature and maintaining vital functions. Urine alkalinisation with forced diuresis and the use of cholestyramine need more data to be supported. The patient's clinical condition may quickly worsen as in this case.

References

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45. Neonicotinoid poisoning: fatal clothianidin ingestion

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Objective: Neonicotinoids are a new class of insecticides, which act as agonists of the nicotinic acetylcholine receptors in insects. They are considered to have low toxicity in humans, so they have become increasingly used all over the world. There are a few reports in the literature of severe poisoning in humans, after ingestion of a large amount of these insecticides [1]. Various gastrointestinal, cardiovascular, neurological and respiratory signs are expected. Treatment is symptomatic and there is no specific antidote. Mortality is less than 3%. We report a fatal case of neonicotinoid poisoning.
Case report: An 84-year-old man ingested a clothianidin-containing pesticide product and took some tablets of midazolam and tramadol. At home he vomited persistently and 20 hours after ingestion he was admitted to our hospital. On arrival he had abdominal pain, mild bowel sounds, low blood pressure and hypoxia. Laboratory tests demonstrated electrolyte disturbances, elevated lactate, white cell count, glucose, urea nitrogen and creatinine concentration. Despite the appropriate supportive treatment (fluid resuscitation, analgesia, laxatives) his condition deteriorated and he developed respiratory failure. The patient was intubated and admitted in the intensive care unit (ICU). Chest and abdominal computerised tomography (CT) scans and surgical examination were performed due to his worsening abdominal status. He did not require surgical intervention, but the CT showed pneumonia and bilateral pleural fluid. In the ICU he was given supportive care, mechanical ventilation, intravenous antibiotics, and total parenteral nutrition. He was hypotensive which was refractory to fluid resuscitation and he required a high dose of vasopressor support. He developed frequent episodes of tachycardia which required beta-blockers and he became anemic requiring a transfusion. On the 12th hospital day he was extubated, but he had a severe muscle weakness (critical illness polyneuropathy/critical illness myopathy), so we he was provided with non-invasive ventilation (NIV). His laboratory data had improved. Despite maximum supportive care he died of heart failure 15 days after his admission.
Conclusion: Neonicotinoids act quite selectively on insects, but they can cause intoxication in humans. We report a fatal case of ingestion of clothianidin. As in the literature, we found that neonicotinoid poisoning can cause multi-organ complications and can sometimes be fatal.

Reference

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46. Unanticipated sources of methanol poisoning: report of two cases

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Objective: To report two cases of methanol poisoning with unanticipated sources of exposure.
Case series: Case 1. A 29-year-old man with intellectual disability presented with intentional poisoning of alcohol-based handrub. The listed content of the handrub were isopropyl alcohol, glycerine, triethanolamine, citric acid, etc. One hour after ingestion of 500 mL handrub, he was comatose (Glasgow Coma Score [GCS] 3), the blood pressure 111/65 mmHg, and SaO_2 82% (on oxygen). The urine dipstick test revealed large amounts of ketone. The laboratory tests 2 hours after ingestion showed mixed metabolic and respiratory acidosis (pH 7.28, PCO_2 7.5 kPa, PO_2 10.2 kPa, base excess −2 mmol/L), normal anion gap (AG) (5 mmol/L), but high osmol gap (OG) (131.5 mOsmol/kg). Serum ethanol was undetectable. Toxic alcohol screening revealed serum concentrations of isopropanol 55.9 mmol/L and methanol 72 mmol/L. Mixed isopropanol and methanol intoxication were diagnosed. Acute haemodialysis, folinic acid and ethanol infusion were commenced. Analysis of the handrub solution revealed a content of isopropanol 36%, methanol 22%, and ethanol 3.5% (gas chromatography with flame-ionisation detection [GC-FID]). Case 2. A 52-year-old man with a history of Kennedy's disease was found comatose in the street with a strong lacquer thinner smell. Physical examination in the emergency department showed impaired consciousness (GCS 9), high blood pressure (190/99 mmHg), fast atrial fibrillation (142 bpm), tachypnoea (respiratory rate 30/min) and desaturation (SaO_2 92% on oxygen). The laboratory tests showed metabolic acidosis (pH 7.09, PCO_2 5.5 kPa, PO_2 11.5 pKa, base excess −18 mmol/L). Serum ethanol, paracetamol and salicylates were undetectable. He was managed in the intensive care unit with airway intubation. The AG and OG determined 8 hours after admission were 14 mmol/L and 52 mOsm/kg, respectively. The serum methanol colorimetric screening test result was positive. He was treated with acute haemodialysis followed by continuous veno-venous haemofiltration and ethanol infusion. Confirmatory analysis by GC-FID revealed a serum methanol concentration of 26 mmol/L. The urine and serum specimens revealed the presence of methanol, acetone, isopropanol and toluene (GC-FID, gas chromatography-mass spectrometry).
Conclusion: Despite its uncommon nature, methanol poisoning may occur from an unanticipated source of exposure such as adulterated alcohol-based handrub [1] or lacquer thinner. A high index of clinical suspicion is needed to diagnose obscure methanol poisoning in patients with unexplained metabolic acidosis.

Reference

[1] Chan GCK, Chan JCM, Szeto CC, et al. Mixed isopropanol-methanol intoxication following ingestion of alcohol-based hand rub solution. Clin Nephrol. 2017;88:218–220.

47. Intractable gastrointestinal symptoms and neuropathies in a patient with ethylene glycol poisoning

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Objective: We present an ethylene glycol (EG) poisoned patient with intractable gastroparesis, long-lasting constipation and multiple cranial and peripheral neuropathies.
Case report: A 53-year-old man with a history of hypertension and schizoaffective disorder was brought to our department. He ingested 0.3-0.4 L of 70% EG solution 5 days earlier in a suicide attempt. On admission he was awake, and oriented to time and place. He was tachycardic (136/min), but other vital signs were normal. Physical examination revealed no abnormalities, but he was anuric. Venous blood gas showed metabolic acidosis (pH 7.234, bicarbonate: 8.7 mmol/L, anion gap 32.8). EG was undetectable in serum. Laboratory studies confirmed acute renal injury (serum creatinine 565 µmol/L). He was started on intermittent haemodialysis (IHD). On day 13 of admission he complained of difficulty swallowing, 2 days later he noted tinnitus, hypacusis, dizziness, numbness and weakness of lower limbs. Otolaryngology and neurological assessment established bilateral palsies of cranial nerves VIII, IX, and X and diminished reflexes, tactile and algetic hypaesthesia, and ataxia of lower limbs with normal muscle force. Computerised tomography of the brain showed no pathology. On day 19 of admission he developed respiratory failure and required mechanical ventilation for 12 days in the intensive care unit (ICU). Tracheotomy was performed. The patient received antibiotics for bronchitis and transfusion. After he was discharged from ICU his hearing and movement improved significantly. He was able to swallow, but complained of persistent nausea and vomiting after meals [1]. His symptoms partially respond to antiemetics; hence he was given a motilin receptor agonist (erythromycin) for 10 days to accelerate gastric emptying [2]. His gastroparesis recovered, but he suffered from constipation and needed laxatives for months. IHD was ceased in 12 weeks, but there was some residual renal impairment and the neuropathy of the lower limbs persisted. He was transferred to the psychiatric department.
Conclusion: Neuropathies and gastroparesis are known delayed neurological sequelae of EG toxicity, but physicians should consider long-lasting constipation as a delayed autonomic nervous system dysfunction. This case illustrates that intractable gastroparesis can be treated successfully with erythromycin in patients with EG poisoning.

References

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[2] Camilleri M, Parkman HP, Shafi MA, et al. Clinical guideline: management of gastroparesis. Am J Gastroenterol. 2013;108:18–38.

48. Liquid laundry detergent pods: analysis of the results obtained from additional information collected during follow up by an Italian Poison Control Centre

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Objective: The Milan Poison Control Centre observed an increase in pediatric exposures to liquid laundry detergent pods but also an increase of number of liquid laundry detergent pods sold during the year 2017 compared to 2016 and we thought it useful to analyze questions to explore behaviors in the home that contribute to incidents.
Methods: Data was collected from 1 January 2018 to 30 September 2019. The questionnaire consists of 21 items, of which 16 are multiple choice and 5 are open, divided into two topics: "General" including age, sex, time of the accident, product, relationship to child involved in the incident, whether the incident happened in or out of the home, the room where the incident happened, if this is where washing machine is kept, and if other children were present in household when incident occurred. "Access description": access occurred from the place of normal storage, or access happened during the laundry task when the carer was using the product and if the product was out of storage or access happened before new pack was put away following a shopping trip.
Results: During the study period, 109 additional information follow up cases were collected. Of these, 45.9% (n = 50) were female and 54.1% (n = 59) were male. The age group distribution was: less than 1 year (n = 1; 0.9%), 1-4 years (n = 95; 87.2%), and 5-8 years (n = 13; 11.9%). The accident happened in the morning (n =2 6; 23.8%), afternoon (n = 35; 32.11%), evening (n = 37; 33.9%), and night time (n = 11; 10.1%). The incident happened most commonly in the bathroom (n = 68; 62.4%), followed by the laundry room (n = 23; 21.1%), kitchen (n = 7; 6.4%), balcony (n = 4; 3.7%), and other (n = 4; 3.7%). The incident occurred most commonly because the child opened the original box (n = 33; 33.0%), the pods were left outside the original box (n = 28; 25.7%), or were taken from the opened box (n = 22; 23.0%). The pods were occasionally taken from inside the drum of the washing machine (n = 14; 12.8%) and the circumstances were unknown in 6 cases (5.5%).
Conclusion: From the data analysis it is clear that the perception of the hazard represented by liquid laundry detergent pods is underestimated. This study showed that parents usually stored the detergent pods in a place accessible to children. Therefore it is clear that providing information to parents to store these products correctly is useful.

49. Laundry pod exposure in children: evaluation of 17 years' of cases in a tertiary care hospital in Italy

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Objective: Liquid laundry detergent pods were first marketed in Europe in 2001. In literature reports laundry detergent pods are considered to pose a serious poisoning risk to young children: it is noteworthy that in Italy laundry pod exposure is 4 times more frequently correlated to pathologically documented lesions compared to other detergents. In this study we aim to analyze 70 cases of pediatric patients that were admitted to the Emergency Department (ED) of "Bambino Gesù" Children Hospital, between 2001 and 2018, due to laundry pod exposure.
Methods: A retrospective study of data collected from the electronic database of the Pediatric Poison Control Center of "Bambino Gesù" Children Hospital. Patients presenting at EDs with injuries involving various detergents were selected. The frequencies produced from this database are estimates based on the statistical weight of the sample. The narratives for each observation were searched for the following words: pod, packs, capsule and ball [pod, ecodose, capsula, sfera, in Italian]. Each case was reviewed to determine if it involved a dissolvable, single use pod. Among all, 70 observations were categorized as documented pod-related clinical cases.
Results: Our data show that pods do not present any additional risk when the exposure concerns children older than one year: no gastric lesion greater than Zargar grade 1 was reported in two children. Instead in the first year of life, exposure may correlate with Zargar grade 2 esophageal lesions (4 cases), acute respiratory distress syndrome (ARDS) (1 case), oral ulcers (1 case) and pathologically relevant lesions can affect approximately 20% of symptomatic patients. Symptomatology broadly conceived is predictive for lesions, while no specific symptoms correlate with specific lesions or grade of severity.
Conclusion: According to our experience, in children less than one-year-old pod exposure should be treated differently to other detergent exposures and endoscopy is recommended when the patient is symptomatic.

50. Self-made mixture "Cobra" poisonings in Lithuanian prison

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Objective: Most substances that can cause abuse are forbidden in prison. Despite this there are many possibilities to use ordinary household items [1] that are available in prison [2] "to get high". A mixture of tobacco, rodenticides and solvents for abuse has not been reported as a reason of severe poisoning in the available medical literature. We would like to report two cases of smoking a mixture of tobacco with solvents and rodenticides that is called "Cobra". Mixing tobacco in different proportions with substances mentioned above seems to be quite common in Pravieniškės Correction House-Open Prison Colony.
Case reports: Two patients were admitted to the Emergency Department of Hospital of the Lithuanian University of Health Sciences Kauno Klinikos. The first was a 21-year-old male who developed coma after generalized convulsions. After 12 hours of supportive care his status improved and after 20 hours he was discharged from the Emergency Department. The second patient was a 32-year-old male who presented with more severe clinical findings: coma, convulsions and respiratory failure and was admitted to the Intensive Care Unit. In this case lung ventilation was necessary for three days, and the patient stayed in hospital for five days. Both patients were transported back to Prison Colony after treatment. The toxic agent was reported by the staff of Prison Colony and by the patients themselves. Toxicologic investigations were not performed.
Conclusion: Abuse of different chemical substances by prisoners is quite common, sometimes by self-made narcotics. Severe intoxications by the mixture of tobacco, rodenticides and solvents can cause convulsions, respiratory depression and unconsciousness.

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51. Artificial nail primer: a case series from Pavia Poison Control Centre

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Objective: The trend for a semi-permanent manicure and the use of acrylic enamelled nails has grown since it guarantees long-lasting adhesion and high resistance. The first step of the whole procedure requires the nails to be cleaned and degreased to ease the adhesion of semi-permanent enamel or artificial nails. For this reason, nail primer, typically containing methacrylic acid, is normally used [1]. We analysed cases reported to our poisons centre.
Methods: All the Pavia Poison Control Centre medical records from January 2007 to August 2019 were retrospectively analysed and searched for the keyword "nail primer". For each included case demographic data, circumstances of exposure, agents involved, clinical picture (expressed with the Poison Severity Score [PSS]), laboratory investigations, treatments, clinical follow-up and outcome, were studied.
Results: Overall 41 patients met the inclusion criteria. The mean age (±SD) was 7.01 ± 9.93, mode 2 years; 29 patients were female. Cutaneous contact was the most common route of exposure (n = 18) followed by cutaneous + buccal contact, buccal contact and ingestion. The majority of patients (90%) presented symptoms (PSS 1) after exposure to nail primer. The main symptoms were 1st degree burns, hyperaemia and local pain; no systemic symptoms emerged. All the lesions were treated symptomatically with a topical antimicrobial unguent or oral gastroprotectants. Methacrylic acid was present in 21 formulations of nail primer out of 23, and induced symptoms in 18 cases. Three cases represented a professional accidental exposure to nail primers; three professional beauticians poured the product on their legs while they were working. All the other accidental exposures occurred at home during the application of enamel nails, or because children accessed the nail primer.

Conclusion: It is important to raise awareness about the risks of using nail primers at home. Indeed, even in normal use of these products, spillage or accidental exposure of children to nail primers can cause health problems and chemical burns, especially following cutaneous or buccal contact. Methacrylic acid is a chemical compound which requires precaution when handled. Moreover, the labels of the product do not always display adequate hazard symbols.

Reference

[1] Woolf A, Shaw J. Childhood injuries from artificial nail primer cosmetic products. Arch Pediatr Adolesc Med. 1998;52:41–46.

52. Nail glue: a beauty hazard

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Objective: Cosmetics are usually considered safe even if sometimes they can cause health problems, especially if misused or left unattended in the vicinity of children. Nail glue, often used also as false eyelash adhesive, is generally made of cyanoacrylate and even accidents during normal use can cause first to second degree burns and cutaneous erythema [1]. We analysed cases reported to our poison centre.
Methods: From 1 January 2007 to 31 August 2019 all patients managed by the Pavia Poison Control Centre (PCC) with a definite exposure to nail glue or false eyelash glue were retrospectively analysed. All the included cases were assessed for age, sex, circumstances of exposure, product composition (if available), and clinical picture expressed with the Poison Severity Score (PSS).
Results: Overall 41 patients, whose age ranged from 1 to 47 years (mean 14.3 ± 13.1, mode 2 years), were evaluated; 71% of patients were female. The most common routes of exposure were cutaneous contact, followed by ingestion, buccal and ocular contact. Overall 24% of patients were asymptomatic ($n = 10$), while 76% ($n = 31$) presented symptoms which were of different severity according to the routes of exposure. Severe lesions were caused by cutaneous contact and ocular contact (PSS 2) and were mainly second degree burns, local hyperemia, glued eyelids and oculodynia. The glue composition was known in 21 cases: in 18 of these, cyanoacrylate was present and was involved in 16 symptomatic cases. In 3 cases the circumstance of exposure was actually a therapeutic error as the patient confused the bottle of nail glue with eye drops. One case was an attempted suicide, two cases arose from a chronic exposure to nail glue, while the remaining 35 cases were caused by accidental spillage of the product during the normal procedure of manicure, or children left unattended who autonomously got hold of the adhesive.
Conclusion: In the last few years this peculiar intoxication seems to be more common thanks to the growing trend of artificial nails and false eyelashes among women and young girls. For this reason, it is important to raise awareness about the possible risks connected with the use of nail glue containing cyanoacrylate.

Reference

[1] Kelemen N, Karagergou E, Jones SL, et al. Full thickness burns caused by cyanoacrylate nail glue: a case series. Burns. 2016;42:e51–e54.

53. Sage oil-induced seizures in a toddler

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Objective: The use of herbal drugs and alternative medicine products has become widespread. *Salvia officinalis* is a plant known as garden sage and it is used for the treatment of various disorders. Sage oil contains well-known convulsant substances such as thujone, camphor and cineole in different proportions. We report a case of a toddler, who experienced generalized tonic-clonic seizures after oral exposure to sage oil.
Case report: An 18-month-old boy with respiratory disease was administered 10 drops of sage essential oil by his mother as an alternative to prescribed antibiotics. Immediately after ingestion, nausea occurred and the boy started to cry. After 30 minutes, flexion of the arms, extension of the legs, abnormal tongue movements, drooling and irregular breathing occurred. At presentation to the emergency department, the child had generalized tonic-clonic convulsion in the hands and arms. A loading dose of 0.3 mg/kg diazepam was administered and the convulsion was stopped. The child had nystagmus and hyperreflexia, noted after termination of the convulsion. He was hospitalized for further investigation. Nystagmus and hypertonicity decreased completely after 24 hours. Neurological examination was normal, as were two electrocardiograms (ECGs), all blood tests, brain computed tomography and magnetic resonance imaging. Viral cultures were negative. The child experienced no convulsions during follow up. The seizures occurred as an isolated event in the toddler.
Conclusion: Although it is widely believed that herbal products are beneficial to health, some herbal products can result in serious adverse effects such as epileptic seizures, especially in children [1]. In any case where the first seizure is of unexplained origin, the possibility of exposure to a herbal product should be kept in mind.

Reference

[1] Halicioglu O, Astarcioglu G, Yaprak I, et al. Toxicity of *Salvia officinalis* in a newborn and a child: an alarming report. Pediatr Neurol. 2011;45:259–260.

54. Suicide attempts using nicotine e-liquids as a new phenomenon in the Czech Republic: a case series

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Objective: Electronic (e-) cigarettes are devices used for evaporating nicotine-containing solutions (e-liquids) to simulate smoking. Concentrations of nicotine dissolved in the mixture of propylene glycol, glycerol, and other components, can be up to 20 mg/L. Since 2012, the phenomenon of acute intoxication due to ingestion or injection of e-liquid from cartridges has been registered by the Toxicological Information Centre. One of the reasons is suicide attempt. Here we present three cases of ingestion of e-liquid with suicidal intent.
Case reports: Case 1. A 34-year-old male with schizophrenia tried to inject e-liquid into the cubital vein. The needle missed the vein and the solution was administered paravenously. The next day he reported what he had done to his psychiatrist during a regular psychiatric examination. No symptoms of poisoning were present and only two haematomas alongside the cubital vein were observed. Case 2. A 56-year-old female injected 20 mL of e-liquid intravenously after ingestion of 0.5 L of vodka and an unknown amount of bromazepam and alprazolam. Four hours later, her children found her unconscious. At admission to hospital she was comatose with Glasgow Coma Score (GCS) 3 (which improved to 6 after 12 hours), pulse 85/min, blood pressure 76/50 mmHg, and oxygen saturation 86%. The patient was intubated and treated with supportive therapy. After improvement with GCS 15 and oxygen saturation 92%, she was transferred to the psychiatry department and discharged 2 days later. Case 3. A 41-year-old male ingested 200 mL of e-liquid (total dose of nicotine 2.7 g) after ingestion of 200 mL of spirits and 8 mg of dosulepin. He vomited immediately and called the ambulance. He was admitted to the hospital within one hour and was treated with gastric lavage, high doses of activated charcoal, intravenous fluids and was discharged the next day after psychiatric examination.
Conclusion: E-liquids present a high risk as toxic substances used in suicide attempts due to their availability and popularity. High concentration of nicotine and easy administration of a potentially lethal dose make this method specifically dangerous. Timely prehospital decontamination measures are crucial to prevent systemic effects and severe poisoning. Long-term health effects in survivors are unknown and lungs may be one of the target organs.

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55. Methemoglobinemia due to ingestion of a car radiator anti-rust product containing sodium nitrite

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Objective: Acquired methemoglobinemia, a life-threatening condition, may result from ingestion of specific drugs or toxins [1], however, it is not easy to diagnose in an emergency setting. Here we report a case of acquired methemoglobinemia in a patient which was diagnosed correctly in our emergency department.
Case report: A 75-year-old female was sent to our emergency department due to acute onset of change in consciousness and dyspnea 2 hours earlier. Emergent intubation was performed because of her respiratory distress. She was transferred to our emergency department for further management. Her Glasgow Coma Score (GCS) was 8 (E3VeM5). On arrival her vital signs were temperature 35 ^{0}C; heart rate 103/min; respiratory rate 22/min; and blood pressure 141/58 mmHg. Pulse oximetry showed desaturation, 85% (on 35% FiO_2). Physical examination revealed cyanotic lips and limbs. The color of a blood sample was chocolate brown. Chest X-ray was unremarkable and an electrocardiogram (EKG) showed sinus rhythm. Arterial blood gas analysis showed: pH 7.35; $PaCO_2$ 36 mmHg; bicarbonate 19.8 mmol/L; PaO_2 314 mmHg; and SaO_2 99%. Saturation gap was noted and the diagnosis of methemoglobinemia was highly suspected. Her methemoglobin concentration was 54.5%. She was given methylene blue (1-2 mg/kg intravenously), regained consciousness, and was extubated successfully. Given the diagnosis of methemoglobinemia, her family was asked to search for possible sources. Two bottles of used car radiator anti-rust agents were found in their refrigerator. The ingredients included ethylene glycol, glycerol, silicates, phosphates, benzotriazole and sodium nitrite. The diagnosis was accidental poisoning due to ingestion of anti-rust agents containing sodium nitrite. The patient was discharged two weeks later without any complications.
Conclusion: Sodium nitrite is widely used as a coloring agent, preservative in food, or ingredient of anti-freezing agents [2,3], and is recognized as a potential cause of methemoglobinemia. Without clear exposure history, cyanosis, chocolate brown colored blood, and mismatch of pulse oximetry and arterial blood gases is highly suspicious of methemoglobinemia. Any nitrite containing chemicals should be considered as a potential cause of methemoglobinemia.

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56. Central pontine myelinolysis in a child with extreme hypernatraemia

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Objective: Extreme hypernatraemia (Na >190 mmol/L) in children is rarely described. Demyelinating syndromes are a rare complication [1]. Management of hypernatraemia is challenging with rapid correction and its complications [2]. We describe a case of central pontine myelinolysis in a child with hypernatraemia.
Case report: A 5-year-old girl with severe global developmental delay and failure to thrive presented to a tertiary paediatric Emergency Department with altered conscious state. The child had been unwell for one week with reduced oral intake, anuria and multiple episodes of vomiting in the preceding 48 hours. On assessment, heart rate was 70 bpm, blood pressure 130/60 mmHg, respiratory rate 32/minute with SpO_2 100% (room air). She was obtunded, profoundly dehydrated and mottled, with global hyperreflexia and clonus. Further assessment revealed that she had been consuming salt and cooking products regularly, with access to kitchen cabinets. She progressed to seizures and brain magnetic resonance imaging (MRI) revealed widespread and likely irreversible supratentorial extrapontine myelinolysis due to severe hypernatraemia. The management was challenging with initial rapid correction of the serum sodium concentration in the first 48 hours with multiple fluid regimens. The child protection unit was involved given the suspected neglect of the child.

Table 1. Laboratory parameters in a child with severe hypernatremia. Endocrinological causes were excluded.

Laboratory parameters	Admission	24 hours	48 hours	5 days
Sodium (mmol/L)	198	147	146	142
Potassium (mmol/L)	2.1	3.5	3.6	3.8
Chloride (mmol/L)	168	139	124	107
Bicarbonate (mmol/L)	16	19.6	21	24
pH	7.32	7.38	7.44	
Urea (mmol/L)	8.5	5.3	4.4	3.6
Creatinine (mmol/L)	49	48	45	38
Urine osmolality (mmol/L)	888	447	–	–
Urine sodium (mmol/L)	494	487	440	–
Serum osmolality (mmol/L)	301	–	–	–
Thyroid function (TSH, free T3, free T4)	Normal	–	–	–
Cortisol concentration (nmol/L)	292	–	–	–
Renin concentration	Normal	–	–	–

She made a slow recovery with involvement of a rehabilitation unit.

Conclusion: Hypernatraemia is a life-threatening medical emergency warranting expert management to prevent complications of a high sodium concentration and its rapid correction [3]. Children with developmental delay are at increased risk of developing hypernatraemia.

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57. Alcohol "abuse" among children younger 5 years

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Objective: Alcohol intoxication is a life-threatening condition and death from alcohol poisoning remains a major concern. The aim of this report is to emphasize improper alcohol usage among children younger than 6 years.

Case series: Case 1. A 3-year-old boy was admitted to Department of Toxicology of "Muratsan" University Hospital on 1 January. His complaints were general weakness, nausea, vomiting (twice). The child's condition assessed fair. Physical examination showed tender abdomen during palpation. At the time of admission respiratory rate was 26/min, pulse 128 bpm, blood pressure 90/60 mmHg, SaO_2 95%. A complete blood count and biochemistry profile were normal. His mother reported that they gave their child champagne to drink on the occasion of the New Year celebration. Diagnosis: alcohol intoxication. Case 2. A 4-year-old girl with loss of consciousness was admitted to hospital with symptoms of general intoxication, progressive illness, vomiting and drowsiness. Physical examination showed pale skin and cold extremities; respiratory rate 24/min, heart rate 120 bpm, blood pressure 90/60 mmHg and SaO_2 95%. History revealed 50-60 mL alcohol usage (mother mentioned that it was advised by neighbor) 30 minutes prior and after drinking the child had vomiting and developed impaired consciousness. Alcohol intoxication diagnosis was made. Case 3. A 5-year-old boy was admitted to hospital with loss of consciousness. He had pale skin and mucous membranes. Physical examination showed tachypnea (37/min) and tachycardia (120 bpm). A biochemistry profile was normal except for hypoglycemia (1.8 mmol/L) [1]. He had had sore throat and fever (38.5 °C) over the previous 2 days and his mother had started a treatment with acetaminophen and cognac. On the morning of admission day she gave him 5 ml of cognac. The blood ethanol concentrations in cases 1, 2 and 3 were 29.6 mmol/L, 34.3 mmol/L and 31.1 mmol/L, respectively. All the children recovered with symptomatic treatment.

Conclusion: There is a mistaken opinion that low doses (evaluated for adults) of alcohol cannot damage children and can even be a cure for some diseases (e.g. tonsillitis) [2]. The most common reasons for alcohol intoxication in Yerevan were celebratory events and inappropriate use of alcohol as a remedy. We conclude that general pediatricians need to have stronger connection with parents to avoid harmful habits.

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58. Sticky eye: a pediatric case of cyanoacrylate ocular exposure

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Objective: Cyanoacrylates are fast-acting adhesives with wide-ranging medical, industrial and household uses. Most cases of exposure involve dermal or ocular exposure, particularly in children less than 5 years of age [1]. This may be due in part to the fact that most cyanoacrylate-containing products are not packaged in child-resistant containers [1]. Although most cases do not result in significant morbidity, ocular exposure can have complications such as corneal abrasion [2]. Currently, there is no standard treatment protocol for ocular cyanoacrylate injuries. Suggested first aid on the packaging often recommends holding the lids open and irrigating with water for at least 15 minutes, but this material undergoes rapid polymerization and frequently there is no time to remove the glue from the eye. Cutting of lashes is generally not necessary. Irrigation with an emulsifying substance can be useful and the use of 3% sodium bicarbonate solution compresses [3] or a Jameson muscle hook, an ophthalmic instrument, has been proposed to treat ocular injuries [4]. We present a pediatric case of ocular exposure.

Case report: A 3-year old girl, presented to the emergency room after nail glue had squirted into her right eye. At examination, the eyelids were glued and there were glue remains on the upper right eyelid and eye lashes. It was impossible to separate the lids, so sterile paraffin oil was used to clean the skin. An ophthalmologist was consulted and he founded the lids closed on the temporal side, partially opened on the nasal side and the

lashes glued and partially detached from the lid edge. Palpation of the lids confirmed normal medial and lateral movement of the globe. Cortisone and antibiotic ophthalmic unguent was administered and the girl was discharged. The local therapy was continued at home and at medical examination 2 days later the lids were opened, with minimal lid swelling and no signs of complications.
Conclusion: In this case, management was conservative and there were no complications. Each case needs individual assessment to determine appropriate management.

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59. The effect of labelling changes on paediatric poisoning with cough and cold medicines: analysis of calls to Australia's largest poisons information centre

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Objective: Over-the-counter (OTC) cough and cold medications include antihistamines, antitussives, expectorants, and decongestants. There is little evidence for the use of OTC cough and cold medications in young children, and severe adverse events and deaths have been reported, resulting in restrictions in several countries. In Australia, compulsory labelling changes were introduced in 2012, stating that medicated cough and cold products should not be given to children under the age of 6, and should only be given to children aged 6-11 years on the advice of a doctor, pharmacist or nurse practitioner. This legislation did not affect herbal cough and cold products. We aimed to evaluate time trends in paediatric poisoning exposures to medicated and herbal cough and cold medications following the labelling change.
Methods: A retrospective study of calls to the New South Wales Poisons Information Centre (NSWPIC, Australia's largest PIC taking 50% of national poisoning calls). Paediatric (<6 years) exposures to cough and cold products were extracted, 2010-2018. Exposures to herbal cough and cold products were also extracted. Calls about medicated products during the 2018 cold/flu season were subject to detailed review of individual case records, to examine the extent of off-label use.
Results: There were 6665 exposures meeting the inclusion criteria. The median (IQR) age was 30 months (24-42 months), 50.5% (3367) were male. Accidental exposures and therapeutic errors accounted for the vast majority of calls (51.6% and 47.2%, respectively). The majority (84.9%) were managed at home. Yearly call numbers for products affected by the labelling change dropped from a mean (SD) of 1049.5 (± 40.3) calls before the change, to 453.0 (± 76.1) following the change. Yearly calls about herbal cold products increased from a mean of 29 (± 0.7) before the change, to 136 (± 48.9) after the change. An analysis of calls during the 2018 cold/flu season revealed 250 eligible calls, of which 92 (36.8%) involved a medication being used for that child therapeutically. The majority (n = 54) were brompheniramine/phenylephrine combinations. Where recorded (53 cases), medications were recommended by doctors in 22, and pharmacists in 17; and parent-selected in 14. Indication was recorded in 52 cases, primarily cold (23), and cough (12 cases).
Conclusion: The 2012 labelling change successfully reduced paediatric poisoning calls about cough and cold preparations, which was partially offset by an increase in calls about herbal products. However, off-label use continues, primarily recommended by healthcare professionals, suggesting that they may underappreciate the risks of these products.

60. Overrepresentation of flavoured, orodispersible tablets in paediatric paracetamol overdoses

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Objective: Overdoses of paracetamol with orodispersible tablets are rare but there has been concern that this formulation may cause unintended overdoses in the paediatric population [1]. Among young children accidental overdoses are, by far, the most common intoxication scenario. In small children a few tablets may be enough for a toxic dose and as orodispersible tablets are often flavoured there is a risk that children could mistake them for candy. In Sweden, orodispersible paracetamol tablets are available over-the-counter and in two versions; 250 mg (strawberry flavour) and 500 mg (blackcurrant flavour). In this report we wanted to investigate whether overdoses with flavoured orodispersible tablets are overrepresented in young children with paracetamol intoxication.
Methods: Hospital calls from 1 January 2018 to 31 May 2019 to the Swedish Poison Centre concerning overdoses with paracetamol in patients younger than 10 years were compared to those concerning patients 10 years and older, including adults. The ratio of overdoses involving orodispersible tablets in the two groups were calculated.
Results: During the study period the Swedish Poison Centre was consulted in 102 cases concerning children less than 10 years of age and in 2317 cases concerning patients 10 years or older. Among the cases of patients <10 years old, 15 of the calls (14.7%), were overdoses due to orodispersible tablets compared to 6 calls (0.25%) in the other group. In 4 of the 15 children with suspected orodispersible overdose the ingested dose was considered safely non-toxic, 11 children were recommended laboratory evaluation and three of these were hospitalised for treatment with N-acetylcysteine. One child developed a slightly increased ALT of 1.51 µkat/L (88.9 U/L) but there were no cases with hepatotoxicity (defined as ALT >17 µkat or 1000 U/L) in either group.
Conclusion: There was a substantial overrepresentation of overdoses with orodispersible tablets in the paediatric population. This indicates that this formulation represents a risk factor for paracetamol intoxication in small children, leading to hospital care, blood test sampling, hospitalisation and antidote treatment

as well as a risk of hepatotoxicity. Orodispersible tablets should have child-resistant packaging and the risk with the formulation should be highlighted to parents, encouraging them to keep medications out of reach of children.

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61. Drug-induced liver injury induced by nicotinamide

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Objective: Nicotinamide is the amide form of vitamin B_3. It is a precursor of essential coenzymes for numerous reactions in the body including adenosine triphosphate (ATP) production. Nicotinamide and nicotinic acid, which is converted into nicotinamide in the body, are subsumed under the term niacin (vitamin B_3). Moderately high supplemental intake of nicotinic acid is associated with flushing and gastrointestinal distress. Long-term use of high doses can also be toxic to the liver. Nicotinamide however, does not cause vasodilation and in general, the risk of nicotinamide toxicity appears to be quite low. We report a child who developed liver toxicity after administration of a high dose of a nicotinamide supplement.
Case report: A 7-year-old boy with epilepsy was admitted to hospital because of repeated vomiting (>20 times daily) for two days. On arrival, he was in poor general condition with dehydration, paleness, and facial petechiae. Laboratory results revealed elevated liver transaminases (AST 2952 U/L, ALT 1886 U/L) and blood coagulation abnormalities (INR 2.4; fibrinogen 148 U/L). Additional testing for infectious etiologies was negative (hepatitis serology for HA, HB and HC, CMV and EBV serology). The parents denied other drugs besides antiepileptic therapy with lamotrigine (300 mg/day) and zonisamide (50 mg/day). On further questioning they admitted also administering nicotinamide (4500 mg/day) during the previous 4 weeks in an attempt to reduce the dose of antiepileptic drugs. The therapy with the over-the-counter (OTC) supplement nicotinamide was recommended in a "Clinic for Bioenergetic Therapy". The intake of nicotinamide was analytically confirmed with an elevated serum concentration of 233 µg/L (reference level 8-52 µg/L). The patient was treated on the intensive care unit (ICU) and supportive therapy consisted of electrolyte and blood volume repletion and substitution of vitamin K. He showed rapid improvement within 4 days, and was discharged from the hospital 3 days later.
Conclusion: Dietary supplements are largely used in children as complementary and alternative medicine to treat different health conditions as in this case. Furthermore, the child was given a 15-fold higher dose (196 mg/kg body weight daily) than the tolerable upper intake for supplemental nicotinamide (12.5 mg/kg body weight daily) over a period of 4 weeks. Nicotinamide-induced hepatotoxicity has very rarely been reported in adults, and appears to be dose-related. In case of acute liver-injury re-evaluation of the anamnesis may be needed, particularly regarding the intake of OTC supplements such as nicotinamide.

62. Availability of the Croatian Poison Control Centre telephone number to parents of preschool children: results of a preventive action

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Objective: To assess the effectiveness of specific poisoning prevention action focused on parents of preschool children.
Methods: Participants were parents of children attending kindergartens under the jurisdiction of City of Zagreb and in Zagreb vicinity. Parents in the intervention group (n = 336) underwent educational intervention during parent meetings which included an oral presentation by the Croatian Poison Control Centre (CPCC) and distribution of gift packages (including a sticker with the CPCC number). Parents in the control group (n = 191) had only a brief explanation about CPCC functions and epidemiology of poisoning in children. Both groups of parents filled out a questionnaire at the baseline (during parents' meetings) and 3 months later (follow-up by telephone). Answers to the question "I have enough information about safekeeping of household products which could potentially cause poisoning of children" were ranked from the safest to the most unsafe as following: "yes", "I cannot estimate", "no". The question about keeping the CPCC number at hand was a yes/no question.
Results: The response rates to follow-up were 74% for intervention and 76% for control group. At the baseline, 64% intervention and 57% control parents stated that they had enough information about safekeeping of household products. At the follow-up, 25% intervention group parents and 27% control group parents changed their answer to a safer category; no significant effect of intervention was noted. At the baseline, 5 parents in the intervention group (1%) and 6 controls (3%) reported keeping the CPCC number by the telephone or in a list of important numbers. Afterwards, 157 parents in the intervention group (64%) started keeping the CPCC number; but only 17 parents reported the same in the control group (12%). Effect was significant even after the adjustment for parents' characteristics as possible confounders (sex, educational level, working status and number of children) by a multiple logistic regression model: intervention versus control OR = 13.06, 95% CI = 7.48-24.03, $p < 0.001$ (P model <0.001, pseudo $R^2 = 0.211$).
Conclusion: Although improvement in parents' estimate of having enough information about safekeeping of potentially harmful products was seen both in the intervention and control groups, indicating that even a short explanation of CPCC functions and frequency of poisoning in children can sensitize parents to this topic, a profound effect of intervention was seen in specific changes of behaviour in parents from the intervention group. After intervention parents recognised the importance of CPCC help in a poisoning incident in a way that was not noted in the control group.

63. Pediatric cannabis poisonings in France: more and more frequent and severe

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Objective: According to the French Observatory for Drugs and Drug Addiction (OFDT), the average content of delta-9-tetrahydrocannabinol (THC) in cannabis resin has tripled in ten years to reach 23% of the final product [1]. The objective was to study the evolution of the number and severity of pediatric cannabis poisoning cases reported to the French network of poison control centers.
Methods: This retrospective study included all cases of ingestion of cannabis among children aged 0 to 10 years reported to the French network of poison control centers from 1 January 2010 to 31 December 2017. The severity of the case was assessed using the Poisoning Severity Score (PSS) [2]. The endpoints for severity were PSS2 or more, admission to intensive care unit (ICU) and respiratory failure.
Results: A total of 966 children were included. The average number of cases was 93 per year from 2010 to 2014 and 167 per year from 2015 to 2017. The median age was 1.3 years (0.25-10 years). In most cases, the poisoning occurred inside the family environment (88%). The ingested form of cannabis was mainly resin (90%). The ingestion of joints/butts, cannabis-based foods, and marijuana accounted for 4.1%, 2.8% and 2.2% of cases, respectively. Most children (79%) had symptoms: hypotonia, agitation, ataxia, loss of consciousness and seizures. Overall, 26.1% ($n = 252$) had a PSS2 or 3, 12.2% ($n = 113$) were admitted to ICU, and respiratory failure was observed in 44 children (4.6%). No deaths were recorded. Comparing 2015-2017 and 2010-2014, there was higher incidence of children with symptoms, a lower Glasgow Coma Score, higher incidence of admission to hospital with a longer stay, and higher incidence for the three endpoints considered ($p < 0.0001$). After adjustment for age, sex and weight of the children, the association between the period 2015-17 (versus 2010-14) with higher severity for PSS and ICU endpoints were still significant ($p < 0.0001$), and of limited significance for respiratory failure ($p = 0.07$).
Conclusion: Between 2010 and 2017, the number of cannabis cases in children and the severity of poisoning increased in France.

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64. Pediatric and adolescent self-poisoning: a 3-year case series

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Objective: Pediatric suicide is a major health problem and remains one of the world leading causes of death among young people [1]. In a Finnish report, 80% of adolescents who attempt suicide have one or more risk factors, both individual and environmental [2]. Among the modalities of self-harm, intoxication is one of the most frequent, especially in females [3]. We analyzed the characteristics of self-poisoning in children and adolescents referred to our Poison Control Centre (PCC).
Methods: Retrospective (2014-2016) observational evaluation of all cases of self-poisoning in children and adolescents (1-18 years) referred to the PCC. Data analyzed included age; gender; known risk factors (e.g. previous self-poisoning, history of psychiatric disorder, alcohol or psychoactive substances abuse, detention in jail or in a therapeutic community); most frequently involved agents; clinical picture; poisoning management; and outcome.
Results: Overall 1488 cases were analysed; 79% were female. Forty patients were younger than 13 years, the youngest was 9-years-old. Known risk factors were present in 23% of cases. Drugs were the main agents involved (74%), followed by domestic, cosmetic and industrial products (26%). In 40% of cases more than one agent was used. Psychiatric drugs accounted for 57% of the drugs (48% of which were benzodiazepines), while acetaminophen accounted for 22%. We observed a high prevalence of female patients in both ingestion of psychiatric drugs (76% of cases) and acetaminophen (85%). Overall 65% of patients were symptomatic: 39% showed gastrointestinal symptoms, 34% neurological and 9% cardiovascular symptoms. Most patients (60%) were treated symptomatically and underwent gastrointestinal decontamination. Only 34 patients (2%) required intensive care unit admission. Antidotal treatment was administered in 59% of acetaminophen intoxications and in 29% of benzodiazepine cases. No death was reported.
Conclusion: We describe an updated national report of self-poisonings in children and adolescents. Clinical effects are mostly of minor severity, since adolescents' principal aim is probably to draw attention. Knowledge of the most frequent agents used, the prevalence in females and the evaluation of risk factors may lead to an improvement in preventive measures aimed at reducing the incidence of this important issue.

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65. Animal PoisonLine: review of a new public access veterinary poisons information service

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Objective: Animal PoisonLine (APL) was launched by the UK Veterinary Poisons Information Service (VPIS) in April 2017 as a triage service providing information to owners concerned their pet may have been poisoned. Payment is via an automated system before advice is given by an Information Scientist. Case histories are obtained, then the owner is either reassured that there is no risk, advised that poisoning is unlikely but they should observe their pet at home and attend the vet if necessary, or advised to attend their veterinary surgery for treatment. Our aim is to ensure owners receive accurate advice and that their pets receive appropriate timely treatment if required. Treatment advice is limited since this may be complex and should be discussed with the treating vet. We evaluated two full years of the service.
Methods: A retrospective study of records of enquiries to APL between 1 September 2017 and 31 August 2019.
Results: Over the study period there were 4,038 calls, 1,218 in "year 1" and 2,820 in "year 2". Of these, less than a quarter of cases (23%, n = 929) were immediately referred to the vet, the remainder were advised there was no immediate danger and the pet could be observed at home, or that the agent involved was not hazardous. Most calls (86%, n = 3,474) involved dogs, the remainder involved cats (11.8%, n = 475), rabbits (1.5%, n = 61) and others (0.7%, n = 27). A third of enquiries (31.1%, n = 1,255) involved human medications, the remainder food (21%, n = 849), household products (13.5%, n = 545), plants/fungi (11.6%, n = 467), pesticides (7.9%, n = 319), veterinary medications (5%, n = 203), garden products (3.1%, n = 127), cosmetics/toiletries (3%, n = 120) and others (3.8%, n = 152). The average call length was 5.49 minutes, compared with 6.17 minutes for VPIS calls. Additionally, 3,040 owners were sent an email survey requesting follow up information; 894 (29%) were returned. Overall 95% of owners reported they were happy with the service. In year 2, 2,820 callers received advice from APL, however a further 1,873 disconnected before or during payment.
Conclusion: The service compliments the current service (VPIS) to veterinary professionals and provides an accurate information source for owners when information found online may be wrong. Call numbers have increased year on year, reflecting the increasing knowledge of the service among vets and owners. The payment aspect of the service remains challenging; in year 2 1,873 callers chose not to pay (40% of the total number of callers).

66. Flurbiprofen toxicosis in dogs

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Objective: Dogs are particularly sensitive to propionic acid non-steroidal anti-inflammatory drugs, including flurbiprofen. In toxicity studies single doses of 1-16 mg/kg caused dose-related gastrointestinal effects [1]. We evaluated clinical signs and outcome of cases of flurbiprofen ingestion in dogs.
Methods: Retrospective analysis of canine flurbiprofen ingestion cases reported to two poison centres, 1983-2018. All cases with exposure to flurbiprofen as a single agent and known outcome were included. Severity was assessed with the Poisoning Severity Score (PSS) modified for dogs.
Results: Information was available for 34 dogs (22 from the UK, 12 from Switzerland). There were 33 cases involving a single dose exposure, of which the dose could be estimated in 21 cases (0.94-248 mg/kg (mean 7 mg/kg). Six dogs remained asymptomatic, five dogs had mild signs, 14 dogs had moderate signs, five dogs had severe poisoning (two were euthanised), three died. One dog had multiple ingestions (1.1 mg/kg for 3 days) and was euthanised. Mild signs reported were vomiting, inappetence and diarrhoea (0.42-80 mg/kg; n = 4). Moderate signs included vomiting (n = 9), diarrhoea (n = 5), haematemesis (n = 4), melaena (n = 4), lethargy (n = 2), anaemia (n = 2), renal impairment (n = 1) and elevated urea and creatinine (n = 1) (0.94-62.1 mg/kg, mean 24.4 mg/kg; n = 8). In severe cases pronounced gastrointestinal signs and evidence of bleeding were prominent; one dog had renal impairment (4.3-248.8 mg/kg; mean 12.8 mg/kg; n = 4). In all fatal cases the dogs had evidence of gastrointestinal inflammation or bleeding, two had gastrointestinal perforation and one had jaundice. Post-mortem examination in a 20 kg dog that died after an unknown dose revealed a huge gastric ulcer, stomach rupture, peritonitis and visceral organ haemorrhage. Where known, dogs with mild signs presented within 2 hours (n = 3) and those with moderate signs within 6 hours (n = 2) or >24 hours (n = 5); in all dogs with severe poisoning time to presentation was not available. Recovery time was 1-7 days. In fatal cases death occurred 5-7 days after ingestion; one dog was euthanised after 5 days and another after 11 days.
Conclusion: In dogs oral flurbiprofen is associated with significant and prolonged gastrointestinal signs with risk of haemorrhage, anaemia and renal impairment. A quarter of dogs had severe signs or fatal outcome. Severity of poisoning does not appear to be dose-related and time to presentation with early supportive treatment may be a more important factor. In this case series the fatality rate including euthanized dogs was 17.6%.

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67. A retrospective study of cement exposure in 42 dogs

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Objective: To determine the typical clinical signs and outcome in dogs exposed to cement.
Methods: A retrospective study of 42 cases of cement exposure in dogs reported to the Veterinary Poisons Information Service (VPIS) between March 2003 and August 2019.
Results: Following cement exposure, 47.6% of cases (n = 20/42) were asymptomatic and their time to presentation ranged from less than 15 minutes to 4 hours. Of the animals that presented with clinical signs (n = 22), vomiting was the commonest sign (45.5%, n = 10/22). Inappetence/anorexia (31.8%), diarrhoea (18.1%) and hypersalivation (13.6%) were other frequently reported effects. Where known, the time of onset of effects ranged from 30 minutes to 12 hours post-exposure. Seven cases involved eye and oral exposure; 28.6% (n = 2/7) developed corneal ulceration, one of which was a Jack Russell Terrier that had torn open a cement bag resulting in ocular burns, corneal ulceration and oral mucosal sloughing. After eight days the eye had healed, but the mouth injury was still apparent, although improving at time of follow up. In another case, a Labrador had clawed and chewed at bags of cement and was found coughing 45

minutes later. Handfuls of cement paste were removed from the dog's mouth. Ocular irrigation and oral lavage were performed, and the dog was repeatedly washed until the skin pH was neutral, which took two hours. Oral inflammation occurred with sloughing of the buccal mucosa and loss of tongue epithelium, which healed in two weeks. The dog suffered no respiratory damage and made a full recovery. In this case series, there was one fatality. A crossbreed presented 4.5-8 hours after tearing open a bag of cement-containing plaster. The dog developed vomiting, hypersalivation, blepharospasm, depression and pharyngeal oedema and was euthanased. Overall, treatment protocols were largely supportive, principally involving copious irrigation of contaminated skin and eyes, and appropriate analgesia.
Conclusion: Cement, which typically contains alkaline calcium oxide or silicate, can cause corrosive injuries to the mouth and gastrointestinal tract, as well as skin and ocular burns. Injuries are often progressive. In this series, 54.8% of dogs developed effects following exposure with the longest documented time to recovery being 2 weeks. Prompt, and potentially prolonged, dermal and ocular decontamination with pH testing, as appropriate, and supportive treatment, including analgesia, are important interventions in case management.

68. Cases of botulism in waterfowls in the Po river valley

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Objective: This work reports on 18 outbreaks of avian botulism in wild and domestic waterfowl, that occurred in the Po river valley (Emilia Romagna, Northern Italy), from 2012 to 2019. Botulism is an intoxication caused by botulinum neurotoxins, which causes a severe flaccid paralysis and death in mammals and birds [1].
Case series: From 2012 to 2019 the laboratories of Bologna, Ferrara and Modena of the Experimental Zooprophylactic Institute diagnosed 18 outbreaks of botulism, equally distributed between domestic and wild waterfowl. The laboratory methods included the detection of the botulinum neurotoxin from serum by mouse test bioassay and/or the detection of botulinum toxin-producing clostridia in intestinal content by RealTime PCR [2]. The bird species involved were: ducks (*Anas platyrhynchos domesticus*), mallards (*Anas platyrhynchos*) in 6 outbreaks each, swans (*Cygnus cygnus*) in 3 outbreaks, Muscovy ducks (*Cairina moschata*), Eurasian teals (*Anas crecca*), moorhens (*Gallinula chloropus*) and egrets (*Egretta garzetta*) in 1 outbreak each, and one outbreak involving both mallards and egrets. The total number of animals involved is not available, particularly for wild birds. For domestic animals, the anamnestic information reported by the owners always included neurological signs of many animals in a short time period. Necropsy always showed non-specific lesions: edema of the subcutaneous tissue, pulmonary congestion, and poor blood coagulation.
Botulinum neurotoxin was demonstrated in serum and clostridia-producing botulinum toxin type C and, only rarely, type CD, were detected in intestinal content by RealTime PCR [2].
Conclusion: Botulism is not a frequent disease but causes great losses among waterfowl populations. It is highly underestimated both in domestic and in wild animals. Often botulinum toxin-producing clostridia grow on the bottom of lakes and ponds making sanitation difficult for the domestic environment and impossible for wetlands so widespread in the Po Valley. Most outbreaks have been detected during summer months, when water temperatures are higher. The climate changes we are witnessing could lead to an increase in cases of botulism.

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69. Perinatal transmission of an anticoagulant rodenticide in a dog

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Objective: Brodifacoum is a second-generation anticoagulant rodenticide with a long duration of action due to enterohepatic circulation and high lipid solubility. It accumulates in the liver with the major route of elimination through faeces. We report a case of perinatal transmission of brodifacoum in a dog.
Case report: A 7.2 kg, 6-month-old Dachshund ingested rodenticide and was treated with vitamin K_1. The dog had a complete resolution of clinical signs by day 9, and remained healthy thereafter. Monthly blood and faecal samples were obtained after the poisoning and analysed by ultra-high performance liquid chromatography–tandem mass spectrometry. A possible new ingestion without effect on coagulation was suspected after blood analysis 1032 days after the first poisoning. On day 1127 (3 years) after the first poisoning and 3 months after the second, she gave birth to four healthy, full-term puppies. Brodifacoum was present in trace amount in the blood 12 days prior to birth, but subsequently not detectable. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were normal. Low concentrations of brodifacoum had been detectable in faeces since the first poisoning, with a brief rise in concentration after the second ingestion. Faecal analyses of brodifacoum in the mother and puppies were obtained using 1 to 3 parallels for each sample with relative standard deviation between 7% and 68% (Table 1). Brodifacoum was detected in moderate concentration in the puppies' meconium. Low concentrations of brodifacoum were detected in the litter of puppies thereafter, for one month after birth. Both mother and puppies remained asymptomatic throughout the study with no evidence of brodifacoum toxicosis.
Conclusion: This is the first case report of anticoagulant rodenticide concentrations in faeces from puppies. Our case demonstrates that residual brodifacoum in the mother can cross the placenta and remains in the puppies for at least one month after birth.

Table 1. Concentrations of brodifacoum in faeces of mother and her litter of puppies before and after parturition.

Day after birth	Animal	Concentration (ng/g)	Parallels	Relative SD
− 12	Mother	13.1	3	13%
1	Mother	219	3	68%
	Puppy	62.7	1	
19	Puppy	3.6	3	9%
23	Puppy	5.5	3	10%
24	Puppy	3.4	3	7%
27	Puppy	4.4	3	9%
28	Puppy	6.0	3	15%
30	Mother	34	3	31%
86	Puppy	Not detected	3	–

70. Suicidal *Cerbera odollam* poisoning: a case report

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Objective: *Cerbera odollam* is a highly toxic plant of the Apocynaceae family. The plant contains cardiac glycosides, including cerberin. *Cerbera odollam* is called suicide tree or pong-pong tree and grows in India, Southeast Asia, Madagascar and the western pacific [1,2]. The seeds are sold via the Internet. We report a case of intentional poisoning with suicidal intent.
Case report: A 19-year-old woman with a panic attack presented to the psychiatric department of a hospital. She had a bradycardia of 35 beats per minute, increasing nausea and repeated vomiting and was transferred to the intensive care unit. After repeated questioning she admitted to having ingested three seeds of the suicide tree with suicidal intent three hours before arrival at the hospital. She had purchased the seeds via the Internet. She was in a poor general condition, somnolent, with ECG changes typical for digitalis overdose with atrioventricular block, partial sinus arrest, ST-segment suppressions and hyperkalaemia (7.4 mmol/L). She was treated with a bolus of digoxin-specific antibody fragments (160 mg IV), followed by a continuous infusion of 160 mg antibody fragments over 20 hours. Hyperkalaemia was treated with insulin/dextrose and furosemide, nausea and vomiting with metoclopramide and fluid replacement. She received colestyramine and activated charcoal to interrupt enterohepatic circulation. Clinical symptoms improved on the second day but the hypotonia lasted several days and she had reduced fluid excretion. Ultrasound examination showed ascites and pleural effusions, possibly caused by the fluid replacement. Thrombocytopenia (83 g/L), anaemia (haemoglobin 10.7 g/dL), and reduced haematocrit (30.4%) occurred on the fifth day. Analysis for cerberin was not available, but digitoxin analysis showed 58.8 ng/mL. The patient's general condition improved on day 6 and she was transferred to the psychiatric department.
Conclusion: This is the first documented case of *Cerbera odollam* poisoning in Austria but due to the availability of the seeds via the Internet, similar cases may occur more often. It is difficult to diagnose this type of poisoning if the patient does not admit the ingestion. In case of unclear bradycardia with suicidal intention, the possibility of *Cerbera odollam* poisoning should be considered.

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71. A 16 year (2002–2017) review of enquiries regarding plant abuse in Austria

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Objective: Many plants have effects which predispose them to recreational misuse. Most of these plants are house or garden plants or can easily be bought online. We reviewed cases of plant abuse reported to our poison centre.
Methods: A retrospective review of enquiries to the Austrian Poisons Information Centre (PIC) concerning plants misused for psychoactive effects was conducted. The extracted data include age cohort, symptoms and Poisoning Severity Score (PSS).
Results: Overall 185 cases (143 male, 40 female and 2 unknown gender), with exposure to psychoactive plants were extracted from the database. The route was oral in 177 cases, inhalation in six cases, and intravenous in two cases. In 58 cases the age of patients was unknown. Five children aged between 13 and 14 years, 26 patients aged 21 to 30 years, and five patients over 30 years were evaluated. The largest group was 91 youths aged between 15 and 20 years. The plants involved in recreational use were *Brugmansia suaveolens* (n = 72), *Argyreia nervosa* (n = 42), *Datura stramonium* (n = 20), *Myristica fragrans* (n = 16), *Atropa belladonna* (n = 8), *Merremia tuberosa* (n = 5), *Ipomoea violacea* (n = 4), *Papaver somniferum* (n = 3), *Ipomoea tricolor* (n = 3), *Mitragyna speciosa* (n = 3), *Salvia divinorum* (n = 2), *Taxus baccata* (n = 2), ayahuasca (n = 1), *Digitalis lutea* (n = 1), *Peganum harmala* (n = 1), *Ricinus communis* (n = 1) and *Sida cordifolia* (n = 1). At the time of PIC consultation 27 patients (14.5%) were asymptomatic. In 57 cases (31%) symptoms were mild (PSS1): nausea, vomiting, diarrhoea, gastralgia, abdominal pain, constipation, vertigo, headache, drowsiness, somnolence, restlessness, mild confusion, paraesthesia, mydriasis, visual disturbances, dyspnoea, mucous membrane irritation, urinary retention. In 99 patients (53.5%) moderate symptoms (PSS2) occurred: nausea, vomiting, drowsiness, somnolence, coma responsive to pain, agitation, hallucination, moderate confusion, muscle fasciculation, seizures, delirium, panic attacks, dysarthria, sinus tachycardia, hypertension, and angina pectoris. Two patients (1%) had severe symptoms (PSS3) with mydriasis, deep coma unresponsive to pain, recurrent generalized seizures and aspiration. Both patients had ingested *Brugmansia suaveolens*. Hallucinations developed in 59 (32%) and agitation in 40 (22%) cases. There were no fatalities.
Conclusion: Drugs of plant origin are easy to obtain, either directly or via the Internet. These "natural drugs" are very interesting for young people and they often like to experiment with them. The majority of cases (54%) had moderate symptoms according to the PSS. Therefore, observation in an intensive care unit may be necessary in some cases.

72. A 16-year (2002–2017) review of suicide attempts by plant ingestion in Austria

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Objective: Many plants contain toxic ingredients and are therefore used for poisoning, including for committing suicide. We review cases reported to our poison centre.
Methods: A retrospective analysis of enquiries to the Austrian Poisons Information Centre (PIC) from 2002 to 2017 concerning monointoxication with plants used in suicide attempts was conducted. The extracted data included misused plants, patient's age, sex, symptoms and Poisoning Severity Score (PSS).
Results: Overall 114 cases regarding suicide with plants were extracted from the database. The route of administration was oral in all cases. Four children (3 girls, 1 boy) aged between 12 and 14 years were involved. There were 110 patients aged 15-65 years (65 females, 44 males and 1 not recorded). The following plants were used: *Taxus baccata* (n = 16), *Convallaria majalis* (n = 15), *Aconitum napellus* (n = 14), *Atropa belladonna* (n = 10), *Colchicum autumnale* (n = 10), *Myristica fragrans* (n = 9), *Digitalis grandiflora/D. purpurea* (n = 7), *Nerium oleander* (n = 7), *Ricinus communis* (n = 6), *Datura stramonium* (n = 6), *Brugmansia suaveolens* (n = 5), *Daphne mezereum* (n = 2), *Veratrum album* (n = 2), *Conium maculatum* (n =1), *Rhus typhina* (n = 1), *Crocus sativus* (safran/saffron) (n = 1), *Laburnum anagyroides* (n = 1), and *Lilium speciosum* (n = 1). At the time of PIC consultation 46 patients (40%) were asymptomatic. In 68 cases the patients had developed symptoms. Symptoms were mild (PSS1) in 42 cases (37%), moderate (PSS2) in 22 patients (19%) and two patients (2%) had severe symptoms (PSS3). There were two lethal cases (2%) involving suicide with *Taxus baccata*. A 35-year-old female patient was found dead at home after ingestion of a large amount of crushed *Taxus baccata* needles. The second lethal case was a 22-year-old woman who died after drinking an unknown amount of an extract of *Taxus baccata* needles. On arrival of the ambulance she was comatose and unresponsive to pain. She had pronounced hypotension, oxygen saturation 50% and became asystolic. The patient was resuscitated for about one hour and treated with adrenaline and a sodium bicarbonate infusion without success.
Conclusion: Plants can easily be used as poisons and women in particular misuse them in order to commit suicide. Some preparations of plants can be very toxic and can be fatal, however, in our analysis only two documented cases out of 114 suicide attempts were lethal. In both cases *Taxus baccata* was involved.

73. Cyanide poisoning after suicidal ingestion of bitter almond

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Objective: Acute cyanide poisoning by voluntary ingestion is rare but can be fatal. Although many plants contain cyanogenic glycosides, food-related cyanide poisonings are rarely reported [1,2]. Bitter almond has been used as a traditional Chinese medicine for a long time. It contains amygdalin which can be catalyzed in human intestine and generate hydrogen cyanide. Swallowing 6-10 bitter almonds may cause serious poisoning, while ingesting more than 50 can lead to death [3].
Case report: A 37-year-old woman was found unconscious in a park and sent to our emergency department by an ambulance. Upon arrival, she was drowsy and disoriented with a Glasgow Coma Score of 10 (E4V2M4). Her vital signs were temperature 35 °C; heart rate 120/min; respiratory rate 20/min; blood pressure 122/70 mmHg. Physical examinations were unremarkable. Laboratory data were as follows: white blood cell count 13,900/μL, blood glucose 372 mg/dL, BUN 16.5 mg/dL, creatinine 1.28 mg/dL, sodium 138 mEq/L, potassium 4.8 mEq/L, chloride 94 mEq/L, serum osmolarity 313, blood ketone bodies 1.6 mmol/L, lactate 136.9 mg/dL, alcohol <10 mg/dL. The venous blood gas showed severe metabolic acidosis with pH 7.063, pCO_2 24 mmHg, pO_2 52.6 mmHg, bicarbonate 6.7 mmol/L, and SaO_2 81%. The anion gap was 37.3. Sodium bicarbonate (100 mg) was given intravenously. She was treated with hydration and continuous insulin infusion under a diagnosis of diabetic ketoacidosis, and admitted to the intensive care unit. She regained consciousness approximate 12 hours after admission and her metabolic acidosis partially improved (pH 7.34, bicarbonate 11 mmol/L). She admitted that she ingested a bag of bitter almond seeds in a suicide attempt. Antidote was not given since she recovered well with stable vital signs. She was discharged on hospital day 5 without sequelae.
Conclusion: Prompt diagnosis of acute cyanide poisoning is critical in order to administer specific antidotes, however, it can be difficult when the exposure history is not provided. In patients rapidly developing unexplained severe lactic acidosis, physicians should think of cyanide poisoning and carefully look for any hint (detailed exposure history, patient's belongings, or the presence of venous arterialization) that support the diagnosis.

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74. Yew (*Taxus baccata*) exposures reported to the UK National Poisons Information Service over 10 years (2009–2019)

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Objective: To investigate the incidence of exposures to yew (*Taxus baccata*) in the UK as reported to the UK National Poisons Information Service (NPIS).

Methods: A retrospective analysis of UK NPIS enquiries between 1 April 2009 and 31 March 2019 was undertaken for enquiries relating to yew exposures.
Results: There were 443 enquiries regarding 427 patients (129 adults and 298 children <18 years of age). The top three sources of enquiry originated from National Health Service (NHS) telephone advice services (n = 142, 32%), hospitals (n = 135, 30%) and primary care (n = 120, 27%). Ages were known in 409 patients, the majority (67%) were under ten years (n = 273) and 232 were under 5 years. Most exposures (n = 331) occurred in the home/domestic settings (77%), public areas accounted for 56 exposures (13%) and 20 exposures (5%) occurred in schools. Occupational exposures accounted for eight cases (2%) and the location of exposure was unknown in 12 (3%). Most exposures (n = 396) were by ingestion (children n = 292 and adults n =104), with 22 (16 of whom were adults) following subcutaneous/cutaneous exposure (including pierced skin and direct skin contact to yew without any personal protective equipment). There were nine exposures to yew via inhalation, all occurring in adults (typically as a result of sawing/burning yew wood). The Poisoning Severity Score (PSS) [1] was known in 417 cases. The majority (95%) of cases had a PSS of either none (n = 329) or minor (n = 69) and seven patients had a PSS of moderate (2%). Twelve patients (including one child) had a PSS of severe at the time of enquiry (3%). Of these 12 cases, the outcome was known in 9 cases, with complete recovery recorded in 5 cases and 4 deaths. All deaths involved intentional ingestions of yew and were characterised by cardiac toxicity secondary to sodium channel blockade.
Conclusion: Yew exposures reported to the NPIS are infrequent, and most exposures occur in children, typically in domestic settings. The majority of exposures result in no or only minor symptoms, however clinicians should be aware that yew exposures, especially intentional ingestions, are potentially life-threatening and although rare, can be fatal.

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75. Near-fatal ricin poisoning by injection

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Objective: To report a near-fatal poisoning after parenteral injection with a castor oil bean extract (*Ricinus communis*) prepared from an Internet recipe.

Table 1. Some major laboratory features in a patient after intentional injection of crushed *Ricinus communis* seeds.

Laboratory parameter	Day 1*	Day 2	Day 4	Day 7
White blood cells (RV: 4-10 × 10^3/mm^3)	12.9	27.9	19.1	25.2
Platelets (RV: 150-400 × 10^3/mm^3)	319	265	52	109
Creatinine (RV <1.2 mg/dL)	0.95	1.5	1.12	1.44
Creatine kinase (RV <170 IU/L)	60	–	2,975	2,985
Troponin (RV <14 ng/L)	3.0	55.2	114.8	56.2
Albumin (RV: 3.5-5.5 g/dL)	3.9	3.0	2.2	1.6
Ricin (serum; ng/mL)[+]	52.4	59.5	2.6	ND
Ricin (urine; ng/mL)[+]	421.8	1,716	269.6	26.5
Ricinine (serum; ng/mL)[+]	12.8	7.3	3.6	0.5
Ricinine (urine; ng/mL)[+]	126.8	77.4	4.0	0.5

ND, not detected; RV, reference value.
*Blood and urine samples (Day 1) were collected 4.5 hours and 14 hours post-exposure, respectively.
[+]Ricin was analysed by ELISA and ricinine by liquid chromatography-tandem mass spectrometry [LC-MS/MS].

Case report: A 21-year-old man (70 kg) crushed approximately 25-30 wild castor oil seeds, mixed them in a saturated salt solution, and self-injected approximately 3 mL intramuscularly and subcutaneously in the left antecubital fossa. Upon emergency department (ED) admission (1 hour later; day 1 [D1]) he was awake and alert, complaining of local pain, with slight local edema and erythema. He evolved to refractory shock (approximately 24 hours post-exposure) that required a large volume of fluids and high doses of norepinephrine and vasopressin, mainly between D2-D4. In addition, he developed clinical and laboratory features compatible with systemic inflammatory response syndrome, multiple organ dysfunction, capillary leak syndrome, rhabdomyolysis and necrotizing fasciitis. There was progressive improvement of the hemodynamic status from D7 onwards. Wound management required several debridements and wound dressings, broad-spectrum antibiotics, hyperbaric oxygen therapy and two skin grafts. Table 1 summarizes some laboratory findings within the first 7 days; there was marked leukocytosis, hypoalbuminemia and increase in troponin and creatine kinase. He was discharged on D71, with limited range of motion and function of the left forearm and hand. Serial analysis of ricin and ricinine in serum and urine detected both substances for several days, with a ricin peak on D2. The ricin concentration in the seed extract was 246 µg/mL, corresponding to the injection of approximately 10 µg of ricin/kg.
Conclusion: Nine reports describing ten ricin poisonings by parenteral routes are available in the medical literature (PubMed, Google Scholar and Conference proceedings; 1964-2019), with nine fatalities. The present case was successfully treated with supportive care and provided important information on ricin toxicokinetics in humans. Ricin detection in urine was unexpected and was probably related to endothelial damage.

76. The effect of hemoperfusion in severe aconitum intoxicated patients evaluated by the serum concentration

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Objective: Although poisoning by *Aconitum* species is reported to cause severe cardiac arrhythmia and mortality, these species are still widely used as herbal medicines in Asia [1]. The benefit of hemoperfusion in patients with severe aconitum poisoning is controversial [2]. We report the relationship of clinical presentations with treatment regimens including hemoperfusion and

serum aconitine concentrations in two patients. Serum aconitine concentration was measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS).
Case reports: Case 1. Ventricular tachycardia/fibrillation (VT/VF) developed after aconitum exposure, and the highest serum aconitine concentration was 6.68 ppb. Extra-corporeal membrane oxygenation (ECMO), and hemoperfusion were performed because of refractory VT/VF under the treatment of defibrillation and antiarrhythmia agents. The patient was discharged without any sequelae. Case 2. Frequent ventricular premature contractions developed when the serum aconitine concentration was 4.9 ppb. Amiodarone, lidocaine and hemoperfusion were administered, and the arrhythmia resolved when the serum aconitine concentration was 2.3 ppb.
Conclusion: Charcoal hemoperfusion was performed in our cases for 3 hours, but the aconitine elimination rate did not accelerate. Our case reports showed that hemoperfusion could not accelerate the elimination of aconitine by analytical confirmation of serum aconitine concentrations. Cases of aconitum poisoning with VT/VF are usually refractory to cardioversion, and early ECMO support is reported to improve survival. In conclusion, our cases demonstrated the serum concentration of aconitine correlated with arrhythmia. When fatal VT/VF develops, early ECMO support could improve survival. Hemoperfusion did not accelerate aconitine elimination in our two cases.

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77. Beauty can occasionally be toxic: local irritation from a houseplant

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Objective: Children are frequently exposed to potentially toxic plants both in the home and outdoors. Since children are curious and readily explore their environment, it is no surprise that they often ingest plant parts including leaves, seeds, berries and flowers. While these exposures rarely result in clinically significant poisoning, it is important for healthcare providers to be aware of the limited number of plants that have the potential to cause significant poisoning and their clinical effects. Children who chew plants of the Araceae family (e.g. *Alocasia*, *Philodendron, Dieffenbachia* [dumbcane]) and other plants that contain calcium oxalate raphides (intracellular sharp projections) may develop mucosal irritation and swelling. Most young children, however, are asymptomatic or have only mild irritation [1].
Case report: A 2-year-old girl was admitted to Toxicology Clinic of Muratsan University Hospital with the following signs: drooling, tenderness and edema of oral mucosa which was assessed as angioedema. Her mother noticed that the child ate a leaf of *Alocasia* and afterwards developed hyperemia of lips and cheeks, oral swelling and drooling. The girl's condition was of moderate severity. Her consciousness was clear, light and gag reflexes were preserved, respiratory rate was slightly elevated. There were no significant changes in other organ systems. Her vital signs were temperature 37 °C, heart rate 130 beats/minute, respiratory rate 32 breaths/minute. A hematology profile showed haemoglobin 111 g/L, red blood cells 3.6×10^9/L, white blood cells 11.8×10^6/L, and erythrocyte sedimentation rate (ESR) 16. A biochemical profile showed aspartate aminotransferase (AST) 30.9 U/L, aspartate aminotransferase (AST) 39.2 U/L, potassium 4.4 mmol/L, sodium 137 mEq/L, and calcium 1.18 mmol/L. The diagnosis of exogenous intoxication by *Alocasia* was made. Treatment was started with oral ibuprofen 10 mg/kg and IV dexamethasone 0.25 mg/kg [2].
Conclusion: Although intoxication by ingestion of this type of plant is usually seen among dogs there is a potential risk to misinterpret irritation and swelling of oral mucosa with angioedema. Symptomatic cases can occasionally be life-threatening, which is another reason to know whether a houseplant is poisonous before keeping it under one's roof with a child.

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78. Hallucinations after ingestion of *Psilocybe semilanceata* in a child

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Objective: *Psilocybe semilanceata* is a common lawn mushroom. Few cases are published describing accidental ingestion of hallucinogenic mushrooms in children. We present a case with moderate toxicity in a child after *P. semilanceata* ingestion.
Case report: A previously healthy 4-year-old girl, 18 kg, ate approximately one cap of a mushroom growing in the lawn in her kindergarten. About 45 minutes after ingestion she developed a sense of exhilaration and hyperactive behavior with giggling and incoherent talk. After one hour, visual hallucinations commenced with visions of blue dogs and spiders, and she heard voices from a turned off television. Her mom also noted that her pupils were dilated. Pictures of three types of mushroom and a berry that the girl might have ingested were retrieved from the kindergarten, and the girl pointed out the mushroom she had eaten. The mushroom was later identified with MMS-photograph as *P. semilanceata* by a professional mycologist working with our poison information centre. At the emergency room, the patient was ataxic and dizzy and she was admitted to the pediatric department for observation. Neurological examination revealed slower reactions, reduced facial expression, and apparent hallucination. Her pupils were mildly dilated, reactive to both direct and indirect light. Vital parameters and laboratory examination including liver and kidney function tests, venous blood gas analysis and electrocardiography were normal. The patient's clinical condition gradually improved over the next 6 hours and she was discharged the next day in good clinical condition. When questioned, she appeared to have partial amnesia of the incident, only remembering the latter part of her hospital stay. Subsequent analysis of urine obtained at the hospital about six hours after ingestion was positive for psilocybin.

Conclusion: Ingestion of *P. semilanceata* in children is uncommon. Our case demonstrates that ingestion of small amounts in pediatric patients can result in visual and auditory hallucinations. Collaboration between poisons centers and professional mycologists is essential in prompt identification and correct treatment after mushroom ingestion.

79. Poisoning caused by self-medication with harmal seeds

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Objective: *Peganum harmala* (harmal, wild rue) grows in Mediterranean areas. Different parts of the plant are used to dye carpets or wool, to protect against "the evil eye" or as recreational drugs. *Peganum harmala* is classified as a noxious weed because its seeds contain the alkaloids harmine and harmaline. These are monoamine oxidase A inhibitors (MAOIs) and increase the effects of psychoactive drugs or are required to make drugs orally active. Combined in an entheogenic brew with dimethyltryptamine (DMT) extracted from *Banisteriopsis caapi,* they are used as a traditional spiritual medicine. Cases of poisoning with this plant when used a traditional medicine have been reported [1,2] and we report a case of poisoning in a child.
Case report: To treat their 12-year-old boy's nocturnal enuresis, parents in La Réunion prepared an infusion with a handful of harmal seeds in half a liter of water. The boy drank one glass of this infusion in the morning and left for school. Arriving at school, he became sick, vomited, presented blurred vision and lost consciousness. An ambulance was called and he was transferred to the emergency department where he presented drowsiness and respiratory acidosis with hypercapnia (pH 7.27, pCO_2 60 mmHg). The electrocardiogram and hemogram were normal. The poison control center was contacted and proposed medical observation with a second arterial blood gas test and another electrocardiogram after intravenous therapy for fluid volume replacement. The boy received the proposed therapy and recovered during the day. The second arterial blood gas test in the afternoon was normal as well as the electrocardiogram, so he was discharged from hospital the same day.
Conclusion: First of all, in our case, the parents used seeds of *Peganum harmala* to treat nocturnal enuresis. After a literature research we did not find nocturnal enuresis as an indication for this treatment. On the contrary, the MAOIs harmine and harmaline achieve the opposite effect: polyuria. Furthermore, his parents were not aware of the negative effects of their treatment, did not keep their son under surveillance and sent him to school, where he lost consciousness. As traditional medicines are used out of context today, people should be conscious of their effects, respect indications and be aware of side effects.

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80. Oxidative storm in a patient with acute yam bean seed poisoning

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Objective: Yam bean (*Pachyrhizus erosus*) seeds contain rotenone, a toxin causing cellular asphyxia via blockage of the mitochondrial electron transport. Subsequent oxidative stress results in lipid peroxidation (LPO). Moreover, the decline in LPO concentrations correlated to improvement of clinical symptoms in a patient with acute poisoning. We report a case of acute yam bean poisoning.
Case report: A 64-year-old woman ate eight pods of yam bean for dinner (around 80 seeds) and presented with vomiting and diarrhea half an hour after ingestion. She complained of dyspnea 2 hours after ingestion and was found unconscious with a Glasgow Coma Score (GCS) of 6 (E1V1M4). Laboratory studies revealed sodium 143 mEq/L, potassium 4.6 mEq/L, chloride 106 mEq/L, creatinine 1.40 mg/dL, alanine aminotransferase (ALT) 36 U/L and lactate 128.7 mg/dL (reference range: 4.5-19.8 mg/dL). Arterial blood gases disclosed pH 7.28, PCO_2 12 mmHg, PO_2 108 mmHg, and bicarbonate 5.6 mmol/L. She underwent a 4 hour course of hemodialysis at around 19 hours post-ingestion. Her consciousness level continually improved with a GCS of 9 (E2V2M5) and 14 (E4V4M6) at 18 hours and 26 hours post-ingestion, respectively. To alleviate oxidative stress, we administered 10 g (150 mg/kg) of intravenous N-acetylcysteine at 25 hours post-exposure, followed by a continuous infusion (50 mg/kg over 4 h and 100 mg/kg over 9 h). On hospital day 3, her consciousness level returned to baseline. Rotenone analysis via liquid chromatography mass spectrometry revealed the following: 31.59 ppm in cooked yam bean seed and 0.1 ppm in the blood. Plasma concentration of LPO increased significantly at 16.5 hours post-ingestion and then decreased gradually with time.
Conclusion: The relationship between rotenone-induced neurotoxicity and reactive oxygen species (ROS) has been investigated in cell line studies [1]. In addition, N-acetylcysteine has chemoprotective activity against rotenone neurotoxicity in cell models [1,2], however, the efficacy of treatment with N-acetylcysteine in humans with acute poisoning is still not known. We enhanced the biological plausibility that an oxidative storm really occurs with yam bean ingestion and encourage the early use of antioxidant agents to alleviate oxidative stress in cases of acute exposures to rotenone-containing plants.

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81. A severe and prolonged case of *Amanita phalloides* poisoning

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Objective: To evaluate the timeline of onset of symptoms and treatment regime in a severe and prolonged case of *Amanita phalloides* poisoning.
Case report: A 50-year old Thai tourist visiting Denmark ingested 3-4 specimens of *Amanita phalloides* resembling a native mushroom of her home region and 18-19 hours later she presented with vomiting and excessive diarrhea. The Danish Poisons Information Centre was contacted 31 hours post-ingestion and a mycologist identified a photograph of *Amanita phalloides* from leftovers (later confirmed). At the nearest hospital she received activated charcoal, G-penicillin and IV crystalloids before transfer to an antidote storing hospital where silibinin was instigated 34 hours post-ingestion and continued for 6 days (Day 1-6). Multiple dose activated charcoal (MDAC) was administered for 3 days (Day 1-3), and acetylcysteine infusion initiated as INR exceeded 1.5 (Day 4-10). On Day 3 uremia and severe acidosis were treated with combined charcoal-hemoperfusion/hemodialysis but acute liver failure on Day 4 led to 17 days in the intensive care unit receiving plasmapheresis (Day 4, 5, 6, 15) and continuous hemodialysis until the INR stabilised. In addition there was persistent renal failure, therefore, a combined kidney and liver transplant may be the only remedy for this patient, although this is ethically challenged by the lack of post-transplant possibilities in the region of origin. At present (Day 43, Table 1) the patient is hemodialysed 3 times a week and is exhibiting a stable INR but increasing bilirubin indicative of little chance of spontaneous liver recovery.
Conclusion: The current Danish regime for *Amanita phalloides* poisoning suggests administration of both MDAC and silibinin for 3 days (G-penicillin, if unavailable) and acetylcysteine if INR >1.5 until signs of liver recovery. Late presentation and delayed suspicion of mushroom poisoning led to late instigation but longer duration of specific antidote treatment in addition to charcoal-hemoperfusion/hemodialysis, plasmapheresis and supportive care; the results of which may call for a revision of the current treatment regime.

82. Experience with mushroom poisoning in a tertiary-care hospital in Latvia: incidence, clinical features and management

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Objective: Mushroom poisoning is the most common botanical poisoning seen in Latvia. We described the incidence and clinical features of mushroom poisoning presenting to our clinical toxicology unit over an eight-year period from 2010 to 2018.
Methods: This is a retrospective descriptive case series of presentations with mushroom poisoning to the Riga Eastern University Clinical Hospital. We determined the incidence of poisoning from various classes of toxic mushroom, clinical features, treatment modalities, mortality rate and hospital length of stay.
Results: There were 111 admissions for mushroom poisoning during the study period, with a gradual decline in yearly presentations over time. Twenty-nine cases were treated in 2010, 18 in 2011, 16 in 2012, 12 in 2013, six in 2014, nine in 2015, six in 2016, 11 in 2017 and four cases in 2018. In the same time period, there were 11,562 admissions for all-cause poisoning. Mean age for mushroom-poisoned patients was 48 years (range: 15-80 years). Fifty-four percent (n = 60) were female. Gastrointestinal

Table 1. Timeline of *Amanita phalloides* poisoning, treatment and biochemical biomarkers in a late-presenting patient.

Dates	Day 0	Day 1	Day 1	Day 1	Day 2	Day 3	Day 3	Day 4	Day 7	Day 21	Day 43
Time	12:00	06:00	20:10	21:57	06:31	02:11	14.58	8:47	05:20	05:44	9:00
Events	Intake	Initial gastrointestinal upset	First Admission	Transfer			HD Charcoal filter	ICU High volume PLEX		Out of ICU	GE ward
Antidote	–	–	Penicillin MDAC	Silibinin MDAC	Silibinin MDAC	Silibinin MDAC	Silibinin MDAC	Silibinin NAC	NAC	Sup. care	Sup. care
ALT U/L (10-45)	–	–	384	–	445	1570	1270	2210	62	42	70
Lactate mmol/L (0.7-2.1)	–	–	1.8	–			9.5	7.6	2.8	2.2	
Bilirubin µmol/L (5-25)	–	–	21	–	37	106	87	90	130	316	436
Creatinine µmol/L (50-90)	–	–	215	–	136	212	271	165	95	417	285
Urea µmol/L (3.1-7.9)	–	–	9.7	–	11.3	14.1	16.9	6.3	3.5	5.8	11.1
INR (<1.2)	–	–	0.9	–	1.0	1.7	3.7	7.3	1.7	2.5	1.8
pH	–	–	7.35	–	–	–	7.09	7.45	7.43	7.49	–
Ammonium U/L 10-45	–	–	–	–	–	–	–	64	76	44	–
Platelets 10^9/L (145-390)	–	–	364	–	278	345	118	24	55	111	99
Hemoglobin mmol/L (7.3-9.5)	–	–	9.2	–	–	9.2	6.2	5.6	4.6	5.0	5.1

ALT: alanine transaminase; HD: hemodialysis; ICU: intensive care unit; INR: International Normalized Ratio; PLEX: plasma exchange.

irritant (GI) mushroom poisoning was the most common reason for admission (73%, n = 81). The most common symptoms reported in all mushroom poisonings were nausea, abdominal pain and diarrhoea. Other classes of mushroom poisoning included: hepatotoxic-amatoxin containing mushrooms (4.5%, n = 5), with liver injury in all five cases, treated with acetylcysteine and silibinin; gyromitrin-containing mushrooms (4.5%, n = 5), with weakness and dizziness, treated with supportive care alone; ibotenic acid-containing mushrooms (7%, n = 8), with weakness and dizziness, treated with supportive care alone; muscarine-containing mushrooms (10%, n = 11), with sweating and bradycardia, treated with supportive care alone; and one case of renal toxic orellanine-containing mushroom poisoning developing acute kidney injury requiring haemodialysis. Median hospital length of stay was shorter for the GI-toxic group (1.3 days) compared to the other toxic mushroom groups (2.8 days). There were no deaths during the study period.
Conclusion: Mushroom poisoning represents a small but significant proportion of patients presenting to our hospital. The GI-toxic mushroom group was the most common class requiring treatment in hospital. While there was only a small number of patients presenting with more toxic mushroom poisonings; most only required supportive therapy. Patients with hepatotoxic and renal-toxic poisoning required organ-specific treatments. The decline in presentations over time is most likely for two reasons. Firstly, recent increasing summer temperatures and drier weather pre-autumn has resulted in less mushroom growth, and secondly, yearly media campaigns have warned the public of the potential risks of mushroom foraging.

83. Poisoning by M'khinza: two cases

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Objective: *Dysphania ambrosioides* (previously *Chenopodium ambrosioides*) commonly known as "Mkhinza" in Morocco [1] is an herbaceous plant belonging to the amaranthaceae family (chenopodioideae subfamily). We report two cases of M'khinza poisoning in two children.
Case reports: Case 1. A 16-month-old child, usually in good health, was admitted to the pediatric emergency room for a disorder of consciousness a few hours after ingesting an undetermined amount of M'khinza, given by his mother as an antiseptic to treat gastroenteritis (diarrhea, vomiting, and fever). On admission, the child was unconscious with a Glasgow Coma Score of 11 with hypotonia. The pupils were equal and reactive without signs of localization. He had perioral cyanosis, blood pressure was 100/60 mmHg, heart rate 140 beats/min, temperature 36 °C and diuresis was maintained. Laboratory tests (complete blood count, blood urea, creatinine, liver function, hemostasis) were normal except for hyponatremia (125 mEq/L). A toxicological analysis was not done. A brain magnetic resonance imaging (MRI) was performed urgently and showed diffuse cerebral and cerebellar white matter abnormalities with cortical signal abnormalities. Treatment was symptomatic with hydration and correction of hyponatremia. The evolution was favourable and neurological disorders regressed in less than 12 hours. Case 2. A 7-month-old child, without particular health history, was admitted to the pediatric emergency room for a disorder of consciousness and persistent fever (40 °C). The history was of poultice application as well as oral administration of an imprecise quantity of M'khinza as an infusion. The child was unconscious with a Glasgow Coma Score of 9, with generalised tonic-clonic seizures. Three hours after admission, the child had bradycardia (36 beats per minute) with a thready pulse, pupils were dilated and diuresis was altered. He was intubated and ventilated and management was symptomatic with vasopressin drug treatment. The evolution was marked by cardiac arrest 18 hours after admission; resuscitation was unsuccessful.
Conclusion: Due to the absence of fundamental studies related to toxicity of this plant, the Poison Control Centre recommends that it is not used in children. In addition, clinicians should discuss the possibility of ingestion of M'khinza in the face of adverse reactions described in the literature [2].

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84. How many hospital visits could have been saved from non-toxic or minor toxic mushroom poisonings: a year review of poisons information centre database in Australia

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Objective: To review mushroom poisoning cases consulted to New South Wales (NSW) Poison Information Centre, Australia from 1 October 2018 to 30 September 2019.
Methods: This is a retrospective review of cases consulted to NSW Poisons Information Centre, Australia from October 2018 to September 2019. Case identification was achieved by electronic searching with the keyword "mushroom". The search was filtered by call type "exposure" and handling type "hospital refer" or "in hospital".
Results: There were 143 mushroom poisoning cases with the cluster size up to 10 patients reported during the study period. Consultation calls were from NSW (56.6%), Victoria (13.3%), Australian Capital Territory (11.2%), Queensland (7.7%), Tasmania (4.2%), South Australia (4.2%) and Western Australia (2.1%). Callers were the general public (40.6%) and healthcare professionals (59.4%) from 85 hospitals throughout the country. The mean age was 16.9 years (range 0.83-93, SD 21). Most patients were male (56.6%). Major types of exposure included accidental (46.9%), intentional (29.4%) and recreational (15.4%). Cases reported from March to June accounted for 93 cases (65%) in total. Average time since exposure to consultation call was 10.9 hours (range 3 minutes to 178.5 hours, SD 20 hours). There were 60 cases (42%) where time from exposure to consultation was 4 hours or sooner. Patients were classified by Poison Severity Score [1] as none (19.6%), minor (54.5%), moderate (22.4%) and severe (0.01%). No fatality was reported during the study period. The severity of four cases was not determined given lack of follow up

data, but fatality was very unlikely according to their initial manifestations. Mushroom identifications were attempted by obtaining fresh samples and/or photos from patients and providing mycologist contacts to the callers, however, no confirmation was reported back whether the mushroom identification was ascertained.
Conclusion: Although fatal mushroom poisonings have been reported in Australia [2], a significant number of cases in this study were considered as non-toxic or minor and could potentially be observed safely at home. An effective triage and mushroom identification network should be implemented nationwide in order to reduce hospital burden and to improve the poisons centre operation.

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85. Facial paralysis after cutaneous burns from *Heracleum mantegazzianum*

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Objective: *Heracleum mantegazzianum* (giant hogweed) is an herbaceous species with potential toxicity. It releases toxic sap which contains phototoxic psoralens, liposoluble substances that can penetrate the epidermis. Once activated by exposure to ultraviolet A (UVA) radiation, they bind to DNA and RNA damaging cell membranes and resulting in phytophotodermatitis causing painful blisters and erythema 48 hours after exposure. These burns may also result in spreading necrosis of the skin and secondary bacterial infections requiring surgical treatment.
Case report: An 8-year-old child was admitted to the emergency department for acute onset headache and pain in right cervical area. The pain was unresponsive to acetaminophen and was followed by the appearance of a movement deficit of the facial nerve (VII cranial nerve), evolving in complete Bell's palsy over 24 hours. Neurologic exam showed facial droop, drooling and dysphagia. Cranial computerised tomography (CT) scan, electroencephalography and ophthalmology evaluation were all normal. All laboratory tests were normal. The history revealed that, 15 days earlier, the child was hospitalized because of a skin burn secondary to accidental contact with *Heracleum mantegazzianum*. The lesion was in the same anatomic area as the pain and improved in approximately 10 days after topical steroid and oral antihistamine administration. Considering the negativity of all the neurological assessments and of all blood tests, including tests for infectious diseases, steroid therapy with prednisone was started. There was some slight improvement after 8 days of therapy. A brain magnetic resonance imaging (MRI), with and without contrast media, was performed 13 days after steroid administration and showed intense impregnation of contrast media of the distal intra-canalicular tract, the geniculate ganglion and of intrapetrosal tract of the VII cranial nerve. These findings are not characteristic for specific neurological pathology and are found in inflammatory diseases of indeterminate nature. Facial nerve paralysis gradually resolved after 19 days of prednisone administration, but complete restoration of its function only occurred 2 months after the first appearance of symptoms.
Conclusion: Considering the involvement of the same anatomical area affected by the lesion from *Heracleum mantegazzianum*, the exclusion of other neurological or infectious diseases, the MRI findings and the improvement after steroid therapy, it is possible to hypothesize that the symptomatology was consequent to an inflammatory reaction triggered by contact with *Heracleum mantegazzianum*. To our knowledge this is the first reported case of Bell's palsy secondary to contact with this plant.

86. Ceylon leadwort (*Plumbago zeylanica*)-induced contact dermatitis and skin erosions

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Objective: Ceylon leadwort (*Plumbago zeylanica*) is used in traditional medicine. We present a case where a patient applied Ceylon leadwort leaves and developed severe contact dermatitis and skin erosions.
Case report: A 56-year-old female was presented to the emergency department with severe painful skin erosions over her posterior neck. She had suffered from cervical vertebral osteophytes-related neck soreness for months and her family suggested a folk remedy which used Ceylon leadwort leaves to relieve the symptoms associated with bony spurs. She developed progressive stinging pain and skin changes, including erythematous vesicles, burn-like erosions, and blackish skin discoloration, just 10 minutes after external application of fresh leaves to her posterior neck. Contact dermatitis was pronounced. She recovered after supportive local treatment and prophylactic antibiotics during admission.
Conclusion: The therapeutic effect of Ceylon leadwort leaves to treat vertebral osteophytes-related symptoms is not based on scientific fact. Severe contact dermatitis and skin erosions after external application to the skin were observed. We strongly recommend not to misuse folk remedies for which therapeutic effects are not clinically approved.

87. Kombucha tea: a potential hepatotoxic agent

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Objective: Kombucha tea (Manchurian tea or Kargasok), is a popular and traditional beverage obtained from the fermentation of a symbiotic culture of acetic acid bacteria and yeasts in a sweet tea. After the inoculum the microorganisms and yeasts aggregate and create a round spongy and slimy pad composed by the microbial biomass, improperly named "mushroom" or more precisely SCOBY (symbiotic culture of bacteria and yeast) which floats on the liquid. Kombucha is said to have healthy properties, even if some case reports pose doubts about its safety and possible adverse effects [1].
Case report: A 31-year-old obese man (BMI 49) with a history of hepatic steatosis and bile duct stones was admitted to hospital for jaundice which had started one week before. History revealed the consumption of homemade Kombucha tea for 7 days before admission. Laboratory evaluation showed hyperbilirubinemia (total bilirubin 27.39 mg/dL, direct bilirubin 24.10 mg/dL), and transaminitis (AST 92 U/L, ALT 60 U/L). Alkaline phosphatase and gamma-glutamyltransferase were normal; serology for hepatotropic viruses was negative. Abdominal ultrasound showed dilatation of the bile ducts: Endoscopic retrograde cholangiopancreatography (ERCP) was performed, after which the patient still had hyperbilirubinemia, although endoscopic control showed complete resolution of the obstruction. Therefore, he underwent an echo-guided liver biopsy that showed, beside a chronic non-alcoholic steatohepatitis (NASH), a canalicular cholestasis with massive neutrophil and eosinophil infiltration. Treatment with ursodeoxycholic acid (1800 mg/day) and N-acetylcysteine (NAC) (300 mg/kg/day) was started. After 15 days NAC was stopped and the patient was discharged with total bilirubin and direct bilirubin values of 14.85 mg/dL and 12.2 mg/dL, respectively. Ursodeoxycholic acid was prescribed for domiciliary therapy. At the two-month follow-up, bilirubinaemia and transaminases were within the normal ranges.
Conclusion: Even if it exists as an industrial product, Kombucha is usually a homemade preparation that could pose considerable health risks due to the impossibility of controlling the products of the bio-fermentation process and even the probable contamination with pathogenic microorganisms. The possible mechanism of Kombucha's toxicity has not been elucidated; however, the timing and onset of symptoms suggest a possible causal association with Kombucha. The role of NAC in the management of symptoms in these cases needs further evaluation. Nevertheless, in consideration of the risk-benefit ratio and the lack of side effects, the therapy was administered.

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88. Does combining vitamin C and vitamin B17 (amygdalin) worsen toxicity?

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Objective: Cyanogenic glycoside ingestion is well reported in the literature. What is infrequently reported is ingestion of specific coingestants to worsen the toxicity of cyanide or cyanogenic glycosides. We report a case of amygdalin ingestion with ascorbic acid in an attempt to increase the toxicity of cyanide.
Case report: A 26-year-old female ingested 10 amygdalin 500 mg tablets and an unknown amount of vitamin C reportedly 24 hours prior to arrival to the emergency department in a self-harm attempt. On initial presentation she was nauseated and reported vomiting once after the ingestion. She reported dizziness and fatigue, but had an otherwise normal exam. Vital signs on presentation included a temperature of 37.3 °C, heart rate (HR) 138 beats/min; blood pressure (BP) 131/67 mmHg; O_2 saturation (SpO_2) 98% on room air and lactate of 3.2 mmol/L. Approximately 5.5 hours after presentation, the patient started vomiting again and repeat vital signs were HR 99 beats/min, BP 103/55 mmHg, SpO_2 95%; repeat lactate was 10.5 mmol/L. Given progressive lactic acidosis and development of hypotension, 5 g of hydroxocobalamin was given intravenously. The patient improved and lactate decreased to 7.2 mmol/L 1 hour later and 1.0 mmol/L after 2 hours. The patient was observed for another 24 hours without any increases in lactate or recurrence of symptoms prior to transfer to a psychiatry unit.
Conclusion: The delayed presentation of cyanide toxicity is consistent with previous reports of amygdalin ingestion. Given the patient developed symptoms 5.5 hours after arrival, it is most likely that she ingested the substance just prior to presentation and not 24 hours prior as reported. Additionally, the patient ingested ascorbic acid in an attempt to worsen toxicity based on her Internet search. Previous studies in guinea pigs found that chronic high dose ascorbic acid depletes cysteine, reducing the conversion of cyanide to thiocyanate resulting in more severe toxicity [1]. Our patient's acute ingestion of ascorbic acid likely did not affect her clinical course. As the Internet continues to play a role in patients' suicide attempts, it is prudent to recognize mechanisms of additive toxicity. Ascorbic acid worsened cyanide toxicity in a guinea pig model, but did not seem to contribute to our patient's course, likely due to the acute ingestion of ascorbic acid.

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89. Confusion between toxic and edible plants registered by the French Poison Control Centres from 2012 to 2018

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Objective: Following a number of alerts from the French Poison Control Centres (PCCs) involving toxic plants being mistaken for edible ones [1,2], the objective was to quantify this issue in order to raise awareness of consumers who pick, grow or purchase plants.
Methods: A retrospective study of cases registered by the PCCs from 2012 to 2018, involving the accidental ingestion of toxic

plants mistaken for edible ones, including children under 6 years of age having shared a meal.
Results: There were 1872 cases of consumption of toxic plants mistaken for edible ones, related to 1159 meals involving 1 to 11 individuals for each meal. Confusion occurred in the summer (32% of the meals), fall (24%), spring (23%) and winter (21%), and mainly concerned bulbs (narcissus, daffodil, crocus, etc.) (12% of the meals), horse chestnut (11%), bitter squash (8.5%), arum leaves (7%), hemlock leaves (4%), cytisus flowers (4%) and black nightshade berries (3.5%). Full information was available in the medical records of 1687 of the 1872 cases (90%). The sex-ratio was 0.8, and the mean age was 39.6 years (from 2 months, for a breastfed child, to 98 years of age). Most cases (53.5%) were symptomatic (n = 903), and most often involved bulbs (21% of symptomatic cases), arum (11%), bitter squash (10%), horse chestnut (9%) and cytisus (8%). Fourteen cases of severe poisoning (PSS 3) were registered, involving colchicum (5 cases), *Veratrum album* (4 cases), *Atropa belladonna* (2 cases), bitter squash (1 case), *Digitalis purpurea* (1 case) and *Oenanthe crocata* (1 case), in addition to a case of fatal poisoning by a hiker who had mistaken aconite leaves for couscouil (*Molopospermum peloponnesiacum*) [1]. While in 90% of the cases people had picked the plants themselves, 5.5% and 4.5%, respectively, purchased or received the plants from a third party.
Conclusion: Since confusion between toxic and edible plants can lead to severe poisoning, the French Agency for Food, Environmental and Occupational Health & Safety, in conjunction with the PCCs, highly recommends that the public clearly identify all plants before eating.

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90. Acute poisoning due to *Datura* ingestion: a case report

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Objective: There is probably no area in clinical toxicology more steeped in folklore, misunderstood, or mismanaged than plant and mushroom poisoning. Although there are thousands of species of plants capable of producing moderate to severe and possibly fatal poisoning, relatively few cases of serious intoxication occur and these are associated with a limited number of plants [1]. *Datura* plants contain dangerous concentrations of anticholinergic tropane alkaloids [2] and *Datura wrightii* is a hallucinogen [3]. We report of a case of *Datura* poisoning in a child.
Case report: A 5-year-old girl was admitted to hospital due to acute intoxication. Her mother noticed that she ate some kind of plant and after 3 hours developed visual hallucinations and became irritable. She had ataxia and her mother complained of inappropriate behavior. Five hours later she was transported to the Toxicology Department of Muratsan University Hospital. On admission her vital signs were respiratory rate 24 breaths per minute, blood pleasure 100/60 mmHg, heart rate 138 beats per minute, oxygen saturation 95%, and temperature 36.6°C. Skin and mucous membranes were pale. No abnormalities were found in the remaining organ systems. The plant was sent to Chair of Botany and Mycology of Yerevan State University and was identified as *Datura wrightii*. Laboratory findings included hemoglobin 132 g/L; red blood cells 4.7 × 10^{12}/L; white blood cells 13.6 × 10^{9}/L; erythrocyte sedimentation rate (ESR) 10 mm/h, aspartate aminotransferase (AST) 26.3 U/L, aspartate aminotransferase (AST) 10.9 U/L; glucose 4.6 mmol/L; potassium 3.8 mmol/L; sodium 135.4 mEq/L; and calcium 1.09 mmol/L. She was treated with intramuscular prozerine and symptomatic treatment was started. After 3 days she was discharged from the hospital fully recovered.
Conclusion: There were no significant changes in laboratory values in this child so proper history taking was an important step in order to establish the correct diagnosis. We conclude that there is a need for parents to be aware of toxic plants growing in their living area. Pediatric toxicologists have to enrich their knowledge arsenal to include hallucinogens which are common in Armenia.

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92. Intoxication with castor beans

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Objective: Although the highly toxic nature of castor oil bean (*Ricinus communis*) is well recognized, reports of human toxicity in the English medical literature are scarce. The potentially lethal doses reported for children and adults are three beans and four to eight beans, respectively [1]. Symptoms of intoxication include acute gastroenteritis, fluid and electrolyte depletion, gastrointestinal bleeding, hemolysis, and hypoglycemia. Delayed cytotoxicity has not been reported [2].
Case report: A 5-year-old boy was admitted to Muratsan University Hospital Complex and complained of vomiting, diarrhea, generalized weakness and dizziness. He had eaten seeds of the castor oil plant and after 40 minutes he started vomiting. On the next day he was taken to hospital. On admission his vital signs were heart rate 132 beats per minute, blood pressure 80/55 mmHg, respiratory rate 24 breaths per minute, temperature 36.2 °C and oxygen saturation 99%. His condition was severe and he had extreme fatigue. Skin and mucous membranes were pale. Laboratory data and ultrasonography did not show any abnormalities. The diagnosis was acute intoxication with castor oil beans. The treatment was symptomatic.
Conclusion: We conclude that there is necessity to increase awareness in parents to prevent their children eating plants which grow in areas they live and are easily accessible.

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93. Severe plant poisonings admitted to the intensive care unit in France: management and outcome

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Objective: Severe poisoning with plants is relatively rare in the urban areas of the European developed countries. Our objectives were to report a series of acute poisonings due to toxic plants requiring intensive care unit (ICU) admission in a university hospital in a large French city.

Methods: We conducted a retrospective single-centre observational study including all plant-poisoned patients admitted to the ICU in 2007–2019. The clinical and biological parameters on admission and at the critical time, the management and the patient outcome were collected.

Results: Twenty-two patients (14 males/8 females, age 33 years [25; 38] (median [25th; 75th percentiles]) were included in the study. Fifteen patients (68%) were admitted following a suicide attempt and 7 patients (32%) for accidental intoxication. The plants involved were diverse mainly including *Ricinus communis* (castor oil plant) (23%), *Taxus baccata* (yew) (18%), *Colchicum autumnale* (autumn crocus) (14%), *Aconitum* species (aconite) (9%) and *Nerium oleander* (oleander) (9%). The main symptoms on ICU admission were vomiting (68%), abdominal pain (41%), diarrhea (23%) and delirium (23%). Seven patients (32%) rapidly developed cardiovascular failure, five patients (23%) manifested cardiac rhythm and conduction disturbances and one patient (5%) presented a sudden cardiac arrest. The patients were treated with activated charcoal (45%), catecholamine infusion (32%), mechanical ventilation (22%), gastric lavage (18%), renal replacement therapy (9%) and veno-arterial extracorporeal membrane oxygenation (VA ECMO) (9%). Two patients (9%) died.

Conclusion: Suicidal or accidental ingestion of toxic plants, even though rare in the Paris area, may result in severe intoxication requiring ICU admission and may even be fatal. Public information is essential to avoid preventable accidents with life-threatening consequences.

94. Cardiac arrhythmia deaths associated with inpatient psychiatric admission and antipsychotic medication

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Objective: Antipsychotic medication is reported to cause QT interval prolongation and torsade de pointes (TdP), which can result in death. In a cohort of inpatients in a public mental health unit, followed for 3 years, we aimed to compare cases of arrhythmogenic deaths to alive controls, to determine any association between arrhythmogenic death and antipsychotic medication exposure during admission.

Methods: We used a nested case-control design for public psychiatric hospital inpatients (January 2001 and December 2010) with data linkage to the Australian National Death Index (NDI). Cases were patients (>18 years) who had died during or within 3 years of their first psychiatric hospital admission, with a primary death codes of I46.1, R09.2, R96, I44, I45, I47, I49 and controls were patients still alive 3 years after discharge. Cases:Controls was 2:1 and were matched for age (10-year window), sex and year of index psychiatric admission. Exposures were medications on discharge, length of stay (LOS), medical comorbidities (using the Charlson Co-morbidity Index (CCI)) and ECGs. Antipsychotic dose was standardised to chlorpromazine (CPZ) equivalent doses.

Results: There were a total of 12,263 psychiatric inpatients within three public facilities over 10 years. Data linkage identified 1,000 deaths within 3 years of hospital admission, of which 6 died from arrhythmia (Table 1). As can be seen in Table 1, of the 6 cases, patients under 65 years had larger doses of antipsychotic medication and longer LOS than controls. However, sequential Cox regression analyses for each exposure variable did not identify any significant relationships between the exposures and arrhythmic death.

Conclusion: Arrhythmogenic cardiac death is a rare outcome in patients who have been admitted to mental health facilities and the lack of a significant relationship between medication use, LOS and comorbidies may be a result of the small number of cases.

Table 1. Characteristics of cases and 2:1 controls examining cardiac arrhythmia deaths associated with inpatient psychiatric admission and antipsychotic medication. Cases were patients (>18 years) who had died during or within 3 years of their first psychiatric hospital admission, with a primary death code of I46.1 (Sudden cardiac death), R09.2 (Respiratory arrest), R96 (Instantaneous death), I44 (Atrioventricular and left bundle-branch block), I45 (Other conduction disorders), I47 (Paroxysmal tachycardia), or I49 (Other cardiac arrhythmias) and controls were patients still alive 3 years after discharge.

Parameter	Cases		Controls		OR	CI	P value
Age (years)	<65 (n = 3)	≥65 (n = 3)	<65 (n = 7)	≥65 (n = 5)	–	–	–
Length of stay, (days), median (range)	12 (12–16)	48 (5–79)	4 (1–44)	15 (6–64)	1.04	0.97–1.12	0.23
Patient on any antipsychotic	3/3	1/3	4/7	3/5	1.30	0.22–7.51	0.77
Chlorpromazine equivalent antipsychotic dose per patient	100 mg 400mg 933mg	20 mg	31 mg 150mg 100mg 500mg	200 mg 30mg 50mg	1.01	0.98–1.01	0.22
Patient on any antidepressant	1/3	2/3	3/7	5/5	0.37	0.04–4.42	0.43
Charlson Co-morbidity Index (CCI) (IQR)	0	2 (1–3)	0 (0–1)	0 (0–1)	14.51	0.04–4745	0.37
ECG present in medical records	0/3	2/3	0/7	4/5	-	–	–

95. *In vivo* comparative CNS antidotal effects of PLGA-loaded pralidoxime nanoparticles and pralidoxime chloride against dimethoate-induced neurotoxicity in BALB/C mice

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Objective: Pralidoxime chloride is the oxime most often used worldwide. It is highly polar which accounts for its poor penetration through the blood brain barrier (BBB). In this present study, poly(lactic-co-glycolic acid) (PLGA)-loaded pralidoxime nanoparticles were compared with pralidoxime chloride for central nervous system (CNS) antidotal effects against dimethoate-induced neurotoxicity in BALB/C mice.
Methods: Pralidoxime-loaded PLGA nanoparticles were prepared using a double emulsion solvent evaporation method. A total of 30, 42 day old male BALB/C mice were randomly assigned to six treatment groups (n = 5) i.e., negative control (normal saline); positive control (atropine only); atropine + pralidoxime chloride (30 mg/kg); and atropine + PLGA-loaded pralidoxime nanoformulation (20, 30 and 40 mg/kg) with each animal having received oral dimethoate 320 mg/kg prior treatment. The Functional Observational Battery (FOB) was used to assess the neurotoxicological effects of diazinon and possible reversal of toxic effects with the different formulations of pralidoxime.
Results: Findings from FOB tests showed that of the groups that were given antidotal treatment the atropine only group had the most severe symptoms and a mortality rate of 80% with a median survival time of less than 6 hours. Reversal of ataxia and sensitivity reactions was noted in the group that was given atropine plus pralidoxime chloride but severe respiratory distress was still present with a 60% mortality rate and a median survival time of 48 hours. Mice given atropine + PLGA-loaded pralidoxime nanoformulations 20, 30 and 40 mg/kg had a reversal of ataxia, excessive sweating, respiratory distress and sensitivity with a median survival time of 72 hours and a mortality rate of 20%, 0% and 0%, respectively.
Conclusion: In this rodent study atropine plus PLGA-loaded pralidoxime had superior antidotal effects compared to pralidoxime chloride and atropine on the reversal of dimethoate-induced neurotoxicity, longer latency period to recovery and seemed to reduce the mortality rate of dimethoate poisoning.

97. Colchicine poisoning: can we predict mortality using a nomogram on hospital admission?

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Objective: Colchicine poisoning is life-threatening and results in a high-rate fatality. Establishing reliable prognosticators on admission is crucial for early identification of patients at risk of death who should benefit from exceptional therapies (e.g. extracorporeal membrane oxygenation (ECMO) or anti-colchicine Fab fragments once available). Although predictive clinical factors have been identified, the exact prognostic value of plasma colchicine concentration (ColC) is unknown. We aimed to assess the prognostic value of ColC on hospital admission and establish a predictive nomogram useful at the bedside.
Methods: We designed a double-centre retrospective cohort study including all colchicine-poisoned patients referred in 1999–2019 to a university hospital intensive care unit (ICU) and a poison control centre (PCC) if i) the ColC on hospital admission was available and ii) the time of ingestion was known. Colchicine poisoning from plant ingestion were not included. We collected all usual clinical and biological parameters on admission and during hospitalization, the complications and final outcome. We determined the predictive factors of death based on univariate comparisons (using chi-squared and Mann-Whitney tests as requested) followed by multivariate logistic regression analyses. We evaluated the prognostic value of ColC related to the time elapsed since ingestion using a multivariate logistic regression model validated by a residual resampling bootstraps approach and Shrinkage index determination. Once the model was validated, we determined the nomogram.
Results: Seventy-two colchicine-poisoned patients (ICU (69%)/PCC database (31%); 45 females/27 males; age, 41 years [25-56], median [25^{th}-75^{th} percentiles]) were included. The presumed ingested dose was 0.45 mg/kg [0.32-0.70]. On admission, the main symptoms were vomiting (71%), tachycardia (59%) and diarrhea (58%). Time from ingestion to hospital admission was 12 hours [6-24] and ColC measured on admission 7.8 ng/mL [4.5-16.5]. The clinical course was characterized by onset of medullary aplasia (42%), renal failure (34%), cardiogenic shock (26%) and acute respiratory distress syndrome (ARDS) (18%); 20 patients (28%) died. Multivariate analysis identified the onset of cardiogenic shock as the only independent mortality prognosticator (odds ratio, 39.9; 95% confidence interval, [2.2-723.4]; p = 0.01). ColC was only predictive if related to the ingested time (area under the curve of the ROC curve, 0.75; [0.63-0.86]; $p < 0.0001$). The c-index issued from bootstrapping (Harrell's c-statistic corrected for estimation optimism) was 0.73, allowing internal validation of the model supporting our nomogram.
Conclusion: Despite optimal supportive management, colchicine poisoning is responsible for high mortality. We established an easy-to-use nomogram at the bedside that reliably predicts the risk of death, by considering the plasma colchicine concentration on admission in relation to the time elapsed since ingestion.

98. Using artificial intelligence to understand recreational drug usage and toxicity from Internet forums

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Objective: The Internet is a vast source of data on the effects and toxicity of recreational drug usage. The scope of Internet data exceeds human capacity to make sense of those data. Machine learning can identify patterns in large data sets, but the statistical relationships it identifies are difficult for clinicians to explain, interpret, or reproduce. The objective of our research is to use artificial intelligence to identify novel usage and toxicity of recreation drug use from the Internet. A secondary objective is to establish the face validity of this approach.
Methods: We have shown that natural language processing of online forums can extract substance-substance and substance-effect co-mentions and that many of these co-mentions reflect patterns of co-ingestion and adverse effects reported in the literature [1]. We applied these algorithms to Lycaeum, an online forum devoted to emerging psychoactive substances to answer three questions: (1) Given mention of substance A, what other substances are also likely mentioned? (2) Given mention of effect A, what other effects are most likely mentioned?, and (3) Given mention of substance A, what effects are most likely mentioned? Clinicians and researchers can interact with this database via the web portal *psychoactive*.
Results: We extracted from Lycaeum discussions of 636 unique substances and 33 effect classes. Of these 636 substances, 257 had no entry in any chemical information database. Of the 201,930 substance-substance co-mentions, 13,604 co-occurred greater than would be expected by chance and 8,942 co-mentions were previously described. Of the 20,988 substance-effect co-mentions, 346 co-occurred more frequently than would be expected by chance and 108 were previously described. Of the 1055 possible effect-effect co-mentions, 540 co-occurred more than would be expected by chance and 502 were previously described. In all cases we computed the likelihood that the conditional probability between substances or effects was significantly greater than zero and then adjusted all p-values to a false discovery rate of 0.05 using the Benjamini-Hochberg correction.
Conclusion: We present here *psychoactive*, a curated database of recreational drug usage and toxicity from online forums. The database contains novel and previously described substances and effects, lending validity to this approach to study known usage and toxicity and track emerging patterns. Psychoactive combines statistical and symbolic artificial intelligence to summarize patterns of use and is open source.

99. The geospatial and linguistic dynamics of conversations on Twitter about vaping

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Objective: The use of electronic nicotine delivery systems (e-cigarettes, "juuls", "vape pens") is a growing public health concern, associated with substance use disorders and, recently, pulmonary injury. Social media provide a means of discussing usage and toxicity. The objective of this study was to determine the geospatial dynamics of discussions about vaping on Twitter.
Methods: We obtained historical tweets from Twitter from 2015-2019 that mentioned any variant of "vape, vaping, #vape, #vaping, juul, or #juul". Twitter provides a 10% random sample of historical tweets to researchers. We calculated the most frequent hashtags each year that contained these search terms. Hashtags are key words users designate by prepending # to the word. We analyzed the metadata of the tweet to identify the postal code from which the tweet originated. We calculated the location quotient (a measure of geospatial inhomogeneity) for vaping tweets for each US postal code. A higher location quotient identifies an area with more discussions on tweets than the national average.
Results: We obtained 411,480 tweets. We excluded tweets with undecipherable or blocked geo-coordinates, leaving 312,198 tweets for analysis. The most common hashtags remained consistently focused on identifying a community of users. In 2015 the top vape-mentioning hashtags were #vape, #vapelife, #vaping, #vapeporn, #vapelyfe. In 2019, the top vape-mentioning hashtags were #vape, #vapefam, #vaping, #vapelife, #vapenation. Twitter discussions were most prevalent in the Eastern United States and more prevalent in the Northeastern and mid-Atlantic region than the Southeast, even after accounting for variation in population (average Getis-Ord Gi, 8.36 for Northeastern versus Southeastern, 6.12 for mid-Atlantic versus Southeastern, 1.31 for mid-Atlantic versus Southeastern). The Getis-Ord Gi is a z-score; values greater than 1.96 indicate significant difference. The variance in the location quotient was stable over time (p-values of F-tests for all combinations of years were >0.10). The top 5 counties with the most Twitter vaping discussion in 2015 were in New Hampshire (1), Maine (2), Connecticut (3,4), and New York (5). In 2019, they were in New Hampshire (1), Maine (2), Vermont (3), Connecticut (4), and New York (5). Parenthesis indicate ranking of counties.
Conclusion: Vaping conversations in the United States have developed a persistent geographic segregation for the East Coast over the last 5 years. The most common vape-mentioning hashtags during this time period remained nearly identical. This is the first analysis of the content and geospatial dynamics of vaping conversations on social media.

100. Poisoning in adolescents

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Objective: To describe enquiries to a national poisons information centre about poisoning in adolescents.
Methods: Data collected routinely during poison centre calls received between 1 November 2018 and 31 May 2019 which related to adolescent patients (10-19 years old) were extracted from the poison centre database and descriptive statistics prepared.
Results: The centre received 510 calls about 481 adolescent patients during the study period; 275 patients (57.1%) were female, 203 male (44.2%) and the gender of 3 patients was not noted. Median age was 15 years and 31.2% were 14-15 years old. The majority of patients aged 10-12 years were male (64.2%) while most 13-19 year olds were female (61.5%). Most exposures (213, 44.3%) were intentional, 117 (24.3%) accidental, 97 (20.2%) therapeutic errors, 33 (6.9%) recreational abuse, 3 adverse drug reactions (6%) and 18 (3.8%) other/unknown intent. Most patients 263 (54.7%) had no symptoms, 163 (33.9%) had minor symptoms, 36 (7.5%) moderate symptoms, and symptoms were not noted or were unrelated to poisoning in 13 cases (2.7%). Six patients (1.2%) had severe features of poisoning: 3 of these were cases of recreational abuse, 2 intentional overdoses and the intent was unknown in 1 case. There were no fatalities. The majority of patients exposed accidentally or during recreational use were male (58.1% and 81.8%, respectively) while 77.5% of intentional cases were female. The median age of patients exposed accidentally or as a result of therapeutic error was 14 years (range 10–19). The median age of the patients exposed intentionally was 16 years (range 13–19) and of those exposed during recreational abuse was 17 years (range 13–19). Accidental exposures mostly involved drugs (41.7%) and household products (30.9%). The majority (91.4%) of intentional exposures involved drugs; 117 of

these patients (54.9%) ingested paracetamol and 68 (31.9%) took other analgesics. Most patients (84.8%) exposed during recreational abuse, 54% of intentional exposures, 31.6% of accidental exposures and 13.4% of therapeutic errors were symptomatic.
Conclusion: Intentional poisoning was the most common reason the poisons centre was contacted about adolescent patients during this study period. Accidental exposure and therapeutic errors were also common causes. Patients exposed accidentally were slightly younger than those exposed intentionally or during recreational abuse. Accidental exposures involved a wider range of products and led to symptoms in a smaller proportion of cases than intentional exposures. The majority of intentional exposures involved female patients who had taken a drug overdose, most commonly paracetamol.

101. Epidemiology of acute exogenous intoxications in children in the Republic of Moldova

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Objective: Epidemiological study of children with acute exogenous intoxications in the Republic of Moldova.
Methods: Retrospective study of data collected by the National Agency for Public Health (NAPH) and the medical records of children who attended the Emergency Department of the Regional Hospital, and/or were admitted to the Mother and Child Institute, 2014-2018. Confirmation of the diagnosis of acute intoxication was made using details of the exact anamnesis, a toxidrome-based approach, and qualitative and quantitative tests for the diagnosis of intoxication [1]. Data was collected on gender, age, etiology and severity of the acute intoxication.
Results: During the study period approximately 5845 children (≤ 18 years) were registered with acute intoxication. They comprised the following groups: up to 1 year 0.4% (n = 26); 1-4 years 45.6% (n = 2669); 5-18 years 52.5% (n = 3130). Adolescents were most commonly involved in voluntary or suicidal intoxications, and children up to 5 years old most commonly involved in accidental acute intoxications. Pharmaceuticals were most commonly involved (n = 2921, 49.9%) followed by alcohol intoxication (n = 863, 14.7%); drugs + ethnobotanicals, psychoactive substances (n = 853, 14.5%); pesticides (n = 234, 4.0%); carbon monoxide and other gases (n = 204, 3.4%); intoxication with household substances (n = 284, 4.8%); mushrooms (n = 156, 2.6%); hydrocarbons (n = 82, 1.4%); plants (n = 25, 0.4%); nitrates (n = 58, 0.9%); and others (n = 165, 2.8%). The latter group included substances such as animal anthelmintics, and preparations used for pediculosis, etc. Most children developed only mild intoxication (n = 2922, 49.9%), and these children received medical care in an emergency department. Serious intoxication was observed in 1808 children (30.9%); and in 1115 children (19.0%) developed severe intoxication, including children that required intensive therapy treatments, treatment in the toxicology department and administration of specific antidotes. There were 22 fatalities (0.37%).
Conclusion: This retrospective study of intoxicated children over a 5-year period indicated that children with acute exogenous intoxication presenting to emergency departments constitute 4.9% of the total number of children managed. We found a substantial prevalence of medicine intoxications, which constituted 49.9%, followed by intoxications with psychoactive substances, drugs and alcohol. These data are similar to the etiological spectrum of intoxications in other European countries in the region and are similar to the specialty literature data [2].

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102. Seizures in a child with confirmed lamotrigine overdose despite levetiracetam loading

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Objective: Paediatric lamotrigine toxicity is rarely reported in the literature [1]. We report a case of accidental overdose complicated by delayed seizures with a confirmed supra-therapeutic serum concentration.
Case report: An otherwise well 2-year-old child (14 kg) ingested 8 mg lorazepam and 600 mg lamotrigine (43 mg/kg), a sibling's medication, during an unsupervised period. After 30 minutes, the parents noted alternating periods of sleepiness and crying, prompting the discovery of the overdose. On arrival to hospital, the child was drowsy but rousable to touch. Vitals were unremarkable. There was no vomiting, abnormal tone or movements. The full blood count, venous blood gas, electrolytes and ECG were normal. Activated charcoal was contraindicated due to drowsiness. Two hours post-ingestion, the child had an episode (lasting <10 seconds) of stiffness, jerking limbs, neck extension and deviated eyes. He was loaded with levetiracetam 20 mg/kg and transferred to the intensive care unit (ICU). One hour later (4 hours post-ingestion), he had 3 further generalised seizures. Next morning, the child was still drowsy, but was fit for discharge at 36 hours. The serum lamotrigine concentration at two hours post-ingestion was 33.7 mg/L (therapeutic range 2.5-15 mg/L). This is towards the higher end of the spectrum of measurements found in children with overdose (3.5-35 mg/L) [1]. The ingested dose of 43 mg/kg of lamotrigine is mid-range for reported paediatric overdoses associated with seizures (range 6.5-72.7 mg/kg) [1,2]. A therapeutic dose is ≤15 mg/kg/day for children under 12 years (product information). In this case, the seizure timing was unusual: the first seizure was at 2 hours 15 minutes (usually <1 hour), and the last at 4 hours post-ingestion (usually <3 hours) [2]. This was despite loading with levetiracetam. Co-ingestion of a benzodiazepine may have been a factor. There were no cardiovascular manifestations of toxicity in this case. Although tachyarrythmias, hypotension and wide QRS are well described in adults, children have only been documented to have sinus tachycardia [1].
Conclusion: In paediatric lamotrigine overdose, seizures may occur later than previously described. The role of levetiracetam in drug-induced seizures needs further study. This case did not demonstrate any cardiovascular toxicity.

References

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103. Mass acute thallium poisoning treated with enteral detoxification using Prussian blue and gut lavage

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Objective: We describe a case of mass thallium poisoning. The incident is under investigation but is thought to have occurred following intentional contamination of an office water cooler with criminal intent.
Case series: Thirty persons aged 37 [33; 43] years were involved. Blood and urine thallium concentrations were determined by inductively coupled plasma mass spectrometry (ICP-MS). In 9 patients assessed as moderately poisoned the maximal thallium blood concentrations ranged from 8.3-26.7 µg/L (benchmark concentration 0.006-0.72 µg/L) and from 48.7-356.1 µg/L in urine (benchmark concentration 0.0-1.0 µg/L). Symptoms reported included sensitivity disorders, tremor (22.2%), vertigo, and impaired walking (33.3%). Seven of these patients were hospitalized to the Poison Treatment Centre. The remaining 21 victims had mild thallium poisoning and blood and urine thallium concentrations varied from 0.3-6.1 µg/L and 2.8-68.5 µg/L, respectively. They complained only of emotional disorders and were treated as out-patients. Alopecia developed from days 17-23. The main therapeutic measures included gut lavage (GL) on the first and second days of treatment using 4.5 liters of saline enteral solution. On the following day Prussian blue was administered orally with laxatives (3 g/day). After a 10-day course of Prussian blue another gut lavage session was performed. During the entire period of treatment (from 9-18 days) all in-patients were given 5 mL intramuscular injection of 5% unithiol (dimercaptopropanesulfonate, DMPS) daily. The 21 out-patients were recommended to be treated at home in a similar way, including Prussian blue. After the treatment the plasma thallium concentration in hospitalized patients ranged from 1.6-9.1 µg/L (a decrease of 69.3%). The urine thallium concentration increased from 9.3 to 59.8 µg/L and the patients were discharged for home treatment. They subjectively noted improvement in their state of health. Patients treated at home were re-examined and also noted a gradual improvement in their condition. Objectively, there were residual effects of motor, sensory, coordinator, emotional and cognitive disorders. Some patients reported regression of tremor and pain.
Conclusion: The clinical symptoms were consistent with acute thallium poisoning and laboratory studies confirmed the diagnosis. The condition of the patients did not require intensive care or hemodialysis. The therapeutic measures including antidotes (Prussian blue and unithiol) and gut lavage were successful. Plasma and urine thallium concentrations significantly decreased and the patients improved. These results allow us to recommend this therapy for mild to moderate thallium poisoning without the use of extracorporeal detoxification methods.

104. Long-term exposure to Sargassum-seaweed pollution in the French Caribbean Islands: clinical consequences and outcome

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Objective: Since early in 2018, there has been an unexplained invasion of Sargassum on the coasts of Caribbean countries [1]. Over an 8-month period, >12,000 cases were reported in Guadeloupe and Martinique. These brown algae are an environmental and economic disaster, and a threat to human health. After 48 hours on shore, decomposition produces large volumes of toxic gases including hydrogen sulfide (H_2S) and ammonia (NH_3). The acute exposure to high H_2S concentrations and can result in potentially fatal hypoxic pulmonary, neurological and cardiovascular injuries; however, the effects of long-term exposure to Sargassum are unknown. Long-term exposures may provoke conjunctiva and upper airways irritation, headaches, vestibular syndrome, memory loss, and modification of learning abilities. Our objective was to evaluate the clinical characteristics and consequences of long-term exposure to Sargassum among the local population.
Methods: A prospective observational cohort study of all patients admitted to the emergency department at the University Hospital, Martinique, March 2018 to December 2018, after exposure to Sargassum. Patients were managed according to the protocol established by the Research Group on Sargassum in Martinique. We assessed exposure and air pollutants using 14 monitors located near of the patient's residence. Demographics and clinical data (including cardiovascular, neurological and respiratory events) were collected. Data are presented as mean ± SD or %. Comparisons were performed using univariate analysis.
Results: In 8 months, 160 patients were included (age: 48 ± 20 years, 54M/146F, past history: hypertension (n = 25), diabetes (n = 29), asthma (n = 14), chronic renal insufficiency (n = 3). Patients arrived with a referral letter from their general practitioner (80%) and presented headaches (76%), developed gastrointestinal disturbances (79%), dizziness (54%), skin lesions (30%), cough (44%) and conjunctivitis (33%). Not all patients were clinically symptomatic. In those presented in June (14%), symptoms more frequently occurred in the workplace or at home ($p < 0.05$). Initial lung function tests were normal (50%). Three patients were admitted to intensive care.
Conclusion: Our study indicates that the magnitude of health effects following long-term exposure to Sargassum may be larger than previously recognized. Efforts to limit long-term exposure are mandatory. Despite the laudable French efforts, a mitigation plan to address this enigmatic Sargassum invasion should be discussed urgently at the international level to boost marine research, pool resources, and conciliate local political priorities.

Reference

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105. Toxicological evaluation of a cluster of reports of hepatitis related to turmeric dietary supplements in Italy

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Objective: Hepatitis related to consumption of dietary supplements is a well know problem. Few reports are published on turmeric-related hepatitis. During 2019 in Italy there was an apparent increase in reports of hepatitis related to intake of turmeric supplements. Curcumin is the principal curcuminoid of turmeric (*Curcuma longa*) which is used a health supplement. Together with the Ministry of Health and Istituto Superiore di Sanità, the risk on public health of these supplements was assessed.
Case series: Overall 23 cases (22 females; age 53 (29-71 years)) of suspected curcumin-related hepatitis referred to the specific Italian System from October 2018 to September 2019 were evaluated. History, clinical, biochemical and instrumental data were collected and evaluated for each case. The causality probability was evaluated using the Roussel Uclaf Causality Assessment Method (RUCAM) score and the World Health Organization (WHO) criteria. All patients had used different supplements containing curcumin for an average period of 98 days (8-730). No patient took more than the recommended daily dose of the supplement. In 10/23 cases (43.5%) the hepatitis was cholestatic, in 8 cases (35%) it was non-specific, but not cholestatic, and in 5 patients (21.5%) it was acute non-specific hepatitis with mild cholestasis. The causality probability evaluated through the RUCAM score was probable in 11 cases (48%), highly probable in 8 (35%) and possible in 4 (17%). The causality probability assessed with WHO criteria considered 13 cases (56.5%) as probable, 9 cases (39%) as possible and 1 (4.5%) certain because of the rechallenge of hepatitis after a second re-exposure to the same supplement.
Conclusion: From October 2018 to July 2019 a significant increase in the incidence of reports of liver damage related to the use of curcumin in Italy was registered. There is no conclusive and well-accepted score to determine with certainty the causal link in these cases. The RUCAM score and the WHO criteria are to be considered useful and gave similar results for these cases. The Italian reporting system has proved its effectiveness. Considering the results of the causality assessment, curcumin might be considered as an infrequent cause of idiosyncratic liver damage. Consequently, further evaluation is needed to assess its safety, at least when administered in relevant doses for a prolonged period.

106. Assessment of advice given by the Danish Poisons Information Centre concerning medication errors in nursing homes and institutions

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Objective: Handling inquiries concerning medication errors in nursing homes and institutions is a core task for the Danish Poisons Information Centre (DPIC). The DPIC is staffed with nurses assisted by an attending physician. The inquiries concerning medication errors are characterized by relatively precise data on medication exposure and timing. The aim of this study was to evaluate the actual advice given by the DPIC and compare this to advice that would have been given if a clinical toxicologist with specific knowledge in pharmaceutical poisonings had been consulted.
Methods: From the 1 March to 16 July 2018 100 consecutive inquiries concerning medication errors were included if 1) they concerned adults living in an institution or nursing home, who had their medication dosed and administered by the staff and 2) a call back to the nursing home or institution generated outcome data (e.g. adverse effects at home or hospital admission). Symptoms and usual medication where recorded if available. All 100 cases were presented in writing to three different physicians with a minimum 3 years of toxicologic experience. All three were blinded to the DPIC advice given, the outcome and the answers of the other clinical toxicologists.
Results: In 81 of the 100 cases there were accordance between both the three clinical toxicologists and the advice given by the DPIC and three hospital admissions were recommended. In the 19 cases without full accordance between the DPIC advice and one or more of the three clinical toxicologists, the DPIC had recommended admission in five situations. In these five cases the three reviewing toxicologists agreed that observation in the nursing home or institution would have been acceptable.
Conclusion: Referral to a hospital was recommended by the DPIC in eight out of 100 inquiries concerning institutional medication errors. Based on post hoc case-analyses these admissions could have been more than halved if a clinical toxicologist had been consulted at the time of the inquiry.

107. Adverse drug reactions (ADRs): improving ADR management for patient safety

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Objective: Increasing comorbidities along with the prescription of multiple medications have increased the complexity of Adverse Drug Reaction (ADR) diagnosis and management. ADR management standards are outlined in the Australian National Safety and Quality Health Service Standards. However, ADR management and review of outcomes are not consistently undertaken. Alfred Health is an 800-bed teaching hospital network and a referral centre, with specialist Allergy and Burns Units. Patients with anaphylaxis and serious dermal drug reactions, such as Stevens-Johnson Syndrome, are areas of interest for the hospital ADR Review Committee. Reporting is actively encouraged, with all reports reviewed by the multi-disciplinary Committee, which has published research on ADR management and epidemiology to inform improvements, with the objective of improving patient safety by minimising harm from ADRs.
Methods: Data from recently published local research in ADR management was mapped to the patient health service journey. Lessons learnt were extracted from each project, to present a systematic approach to ADR management. Quality improvement opportunities were highlighted in staff education, ADR reporting, ADR documentation and patient communication.
Results: Despite a model of active reporting and review, research outcomes indicated several gaps, triggering targeted improvements. Under-reporting of severe ADRs led to introduction with educational sessions of an electronic reporting system in 2017. ADR diagnosis required improvements to ensure more timely diagnosis. Educational activities in drug allergy management and ADR causality are being developed. Documentation of severe

reactions was inconsistent and incomplete across paper-based medical record platforms. Pharmacists now enter ADR and medicines information in discharge summaries. Electronic prescribing was introduced in 2018, with ADR documentation in the electronic medication record as the "one source of truth". Patient follow-up after severe reactions is essential to provide allergy testing and recommendations for future medication use. Antibiotic and anaesthetic allergy clinic referrals enable specialised testing. As patient held information is essential for risk management, written information is sent to patients. E- health options are being investigated.

Conclusion: A conceptual framework for the management of ADRs was mapped to the patient healthcare journey. The main challenges were ensuring all severe ADRs are reported, accurate allergy histories are obtained and new ADRs are appropriately investigated. Other challenges include ensuring ADR education for clinicians amongst competing priorities. Despite no specific resources for ADR Committee activities, research has been actively pursued by its members, informing multiple targeted interventions to improve patient safety.

108. Utilization of the Danish Poisons Information Centre: a nationwide registry study

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Objective: Limited information exists about the utilization of poison information centres (PIC) which is important in assessing the impact of a PIC. In Denmark the Danish Poisons Information Centre (DPIC) opened for the public on 15 August 2006. Hence the aim of this study was to examine the development in the utilization of the DPIC.

Methods: The study population consisted of all cases in Denmark admitted with a diagnosis of a poisoning (ICD10 codes T36-T65, X40-X49, X60-X69, and F100, F110 to F190) from 15 August 2006 to 31 December 2017 and all contacts to the DPIC in the same timeframe. Data were obtained from the Danish National Hospital Registry and the DPIC database. Cases in the DPIC database were linked to the Danish National Hospital Registry using CPR (Central Person Register) numbers, a unique personal identification number given to all Danish residents at birth or upon immigration.

Results: From 2006 to 2017 there were 231,180 enquiries to the DPIC. In 63% of the cases a CPR number was available. In the same timeframe there were 299,160 admissions with a poison diagnosis of which 43,458 (15%) were in contact with the DPIC. An additional 21,432 admissions were also in contact with DPIC but without a poison diagnosis. Details about the poisonings are presented in Table 1.

Conclusion: The utilization of the DPIC has been steadily increasing over the last 10 years. The DPIC is contacted less often for more common poisonings.

109. Non-medical use and injection use of prescription opioids in Europe in the Non-Medical Use of Prescription Drug (NMURx) National Surveys

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Objective: Non-medical use (NMU) and injection use of prescription opioids has been described in Europe; however, cross-country comparisons can be difficult. Using a harmonized questionnaire and sampling methodology, we estimated the prevalence of prescription opioid NMU and injection use in four European countries.

Methods: NMURx is a series of cross-sectional online surveys collecting data from the adult general population on NMU of prescription drugs, demographics, and behaviors. NMU was defined as using a medication in a way not directed by your healthcare provider. NMURx data from Germany (4Q2018, n = 14,959), Italy (4Q2018, n = 9,974), Spain (4Q2018, n = 9,945), and the United Kingdom (3Q2018, n = 9,926) were analyzed. Calibration weighting was applied to represent national adult population distributions. National rates of past 12 month NMU of three opioids (tramadol, morphine, oxycodone) were calculated by country. Injection use behaviours were calculated among those who reported last year NMU.

Results: Estimated rates of opioid NMU were highest in Spain, followed by the UK, Germany, and Italy (Table 1). In three of four countries, the prevalence was highest for tramadol, with an estimated 3,092,234 adults across all countries non-medically using

Table 1. Poisonings in the Danish National Hospital Registry.

Year	2006–2017 Contact with DPIC/total (%)	2007 Contact with DPIC/total (%)	2012 Contact with DPIC/total (%)	2017 Contact with DPIC/total (%)
Poisonings	43.458/299.160 (15%)	2,444/28,180 (9%)	3,863/25,883 (15%)	4,658/21,837 (21%)
Pharmaceutical poisoning	34,511/134,148 (26%)	1,717/12,525 (14%)	3,227/12,135 (27%)	3,681/10,060 (37%)
Alcohol poisoning	2,044/103,001 (2%)	120/10,828 (1%)	195/9,432 (2%)	152/6,298 (2%)
Insect bites/stings	74/30,460 (0.2%)	2/2,390 (0.08%)	4/1,820 (0.2%)	12/1,679 (0.7%)
Weak analgesics including paracetamol	8,378/44,124 (19%)	377/4,232 (9%)	884/4,261 (21%)	799/2,920 (27%)
Age group				
0–10 years	7,206/17,323 (42%)	652/1,847 (35%)	516/1,178 (44%)	515/1,061 (49%)
11–17 years	4,277/29,036 (15%)	297/3,335 (9%)	343/2,359 (15%)	467/1,886 (25%)
18–65 years	29,421/217,217 (14%)	1,391/20,026 (7%)	2,774/19,354 (14%)	3,313/15,993 (21%)
65+ years	2,554/35,584 (7%)	104/2,972 (3%)	230/2,992 (8%)	363/2,897 (13%)
Died within 30 days from admission	314/3,444 (9%)	17/354 (5%)	36/288 (12%)	29/278 (10%)
Admitted to an intensive care unit	4,926/16,544 (30%)	317/1,568 (20%)	523/1,582 (33%)	364/1,028 (35%)

Table 1. Non-Medical Use of Prescription Drug (NMURx) national survey respondents with any opioid non-medical use and injection opioid non-medical use in past 12 months (95% CI).

	Germany		Italy		Spain		United Kingdom	
Opioid	Any NMU	NMU by Injection	Any NMU	NMU by Injection	Any NMU	NMU by Injection	Any NMU	NMU by Injection
	Rate per 100,000 Population							
Tramadol	**1222**		348		**2931**		**1688**	
	(1052-1392)		(248-448)		**(2489-3373)**		**(1459-1917)**	
Morphine	495		**582**		632		953	
	(382-608)		**(454-709)**		(465-799)		(781-1125)	
Oxycodone	444		292		328		331	
	(343-545)		(207-378)		(238-418)		(227-435)	
	Rate per 100,000 Standard Units Sold							
Tramadol	**383**		210		150		118	
	(330-436)		(149-271)		(128-173)		(102-134)	
Morphine	**470**		**2539**		**931**		134	
	(363-578)		**(1983-3095)**		**(685-1178)**		(110-158)	
Oxycodone	131		127		184		126	
	(102-161)		(90-164)		(134-234)		(86-166)	
	Total Weighted Prevalence (% of NMU)							
Tramadol	846,571	46,225	176,321	**46,125**	1,162,976	56,193	906,366	80,111
		5% (2-9%)		**26% (14-38%)**		5% (3-7%)		9% (6-12%)
Morphine	342,809	**100,733**	294,711	**95,385**	250,777	**83,563**	511,778	**106,619**
		29% (19-39%)		**32% (22-43%)**		**33% (22-45%)**		**21% (14-27%)**
Oxycodone	307,405	27,872	148,143	**45,012**	129,981	**23,579**	177,715	**41,908**
		9% (3-15%)		**30% (17-44%)**		**18% (8-28%)**		**24% (12-35%)**

tramadol in the past year. However, the proportion of NMU by injection was highest for morphine in all countries, with an estimated 386,400 adults across all countries. Oxycodone had the second largest proportion of NMU by injection, followed by tramadol.

Conclusion: Of the four European countries studied, Spain had the highest rate of NMU of opioids analysed per population. Despite the differences in baseline rates of opioid NMU, trends were similar across countries. In three of four countries, the rate of NMU per population was highest for tramadol among the three opioids studied, while morphine and oxycodone had the highest proportion of NMU by injection.

110. Pharmacokinetic modelling for anticipating an incomplete response to the recommended dose of idarucizumab

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Objective: Idarucizumab binds to dabigatran to reverse dabigatran-induced anticoagulation. The recommended 5 g dose of idarucizumab is based on data from healthy volunteers and patients with limited comorbidities. Evidence suggests that dabigatran concentrations between 75-240 ng/mL may reflect a therapeutic range. Clinical experience notes failure of this dose in heterogeneous cases with higher dabigatran concentrations. We hypothesised that the dabigatran concentration in the central compartment influences immediate response to idarucizumab, and peripheral compartment concentrations influence the rate and extent of rebound plasma dabigatran concentrations.

Methods: A two-compartment pharmacokinetic model for dabigatran 150 mg twice daily for 7 days was developed in Berkeley Madonna version 8.3.18. Parameters defining the model including absorption rate constant, renal clearance, volumes and inter-compartmental clearance were fixed to literature values. The impact of renal dysfunction on the effect of idarucizumab were explored, based on 100%, 50%, 25% and 5% of normal renal clearance. Acute and chronic renal impairment were modelled identically and both non-renal clearance and oral bioavailability were assumed to be constant.

Results: In patients with normal, 50% or 25% renal function, time to central compartment steady state concentrations were 72, 98 and 120 hours respectively. Steady state was not achieved in those with 5% renal function after 7 days. Peak plasma concentrations for each group were 230, 380, 641 and 1620 ng/mL, respectively. A similar trend was seen in time taken to achieve peripheral compartment steady state concentrations. In normal, 50% and 25% renal function, steady state was achieved in 72, 114 and 140 hours, respectively. Steady state was not achieved in those with 5% renal function after 7 days. Peak peripheral compartment concentrations for each group were 149, 289, 542 and 1440 ng/mL. At steady state and with normal renal function, idarucizumab reduced dabigatran central compartment concentrations from 230 ng/mL to 6 ng/mL. A peak rebound in dabigatran concentrations were seen to 130 ng/mL. Similarly, at 50% renal function, dabigatran concentrations reduced from 380 ng/mL to 199 ng/mL. A peak rebound concentration of 261 ng/mL occurred. At 25% and 5% renal function, concentrations decreased from 641 ng/mL and 1620 ng/mL to 448 ng/mL and 1348 ng/mL, respectively. Peak rebound concentrations of 507 ng/mL and 1417 ng/mL, respectively, were seen.

Conclusion: These data suggest that the recommended dose of idarucizumab may be inadequate to neutralise dabigatran in renal dysfunction, with concentrations returning to levels above the therapeutic range.

111. Pharmacokinetics of high-dose intravenous lipid emulsion: a randomized clinical trial

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Objective: Intravenous lipid emulsion (ILE, Intralipid® 20%) is used in the management of severe poisonings, but distribution and clearance kinetics of high-dose ILE is unclarified. Our objective was therefore to describe the pharmacokinetics of high-dose ILE.
Methods: In a randomized clinical trial, ten participants were administered 5.25 mL/kg ILE over 17 minutes [1]. The components of ILE; triglycerides (TG), free fatty acids (FFA), and phospholipids, were measured from baseline to the 120 min timepoint. Nonlinear mixed-effects modelling was used to define the best model for lipid kinetics. Population parameters (baseline lipid synthesis, volumes of distribution, elimination rate constants and clearances) were estimated from the final models. Ethics approval was obtained for the study.
Results: Immediately after the bolus, TG elimination mechanisms were saturated at TG concentrations of 8-12 mmol/L (an 800-1300% increase from baseline). FFA concentrations increased 180% from baseline to 50 min and remained unchanged to 120 min. A one-compartment disposition model with zero-order kinetics best described distribution and lipoprotein lipase-mediated hydrolysis of TG producing FFA. Phospholipid concentrations increased 70% from baseline to 50 min and decreased negligibly after plateau (at 1600-1700 µmol/L) was reached. Phospholipid pharmacokinetics was adequately described by a one-compartment disposition model.
Conclusion: High-dose ILE rapidly exceeded TG clearance capacity and increased TG and FFA concentrations. FFA concentrations remained constant after the initial increase, indicating equilibrium between cellular FFA uptake and spill-over from lipoprotein lipase-induced TG hydrolysis in tissues. Phospholipid concentrations remained increased after infusion.

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112. Mushroom poisonings in Finland: a 15-year retrospective study

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Objective: To analyse mushroom exposures reported to the Finnish Poison Information Center (FPIC) in relation to mushroom-related poisonings in Finland from 1 June 2000 to 31 December 2015.
Methods: We retrospectively collected and analysed the enquiries concerning poisonous or unidentified mushrooms from the FPIC database. Information on age, gender, time of exposure and clinical effects were collected. We also included data from Helsinki University Hospital on the Molecular Adsorbent Recycling System (MARS)-treated patients and liver transplantations performed due to mushroom poisonings. Statistics Finland provided information about mushroom poisoning deaths in Finland.
Results: FPIC received 10,869 enquiries related to acute human exposure to a poisonous or unidentified mushroom over the study period. Overall, more than a half of the cases (56%, n = 6163) concerned unidentified mushrooms. The most commonly identified mushrooms were *Amanita muscaria* (n = 1350), *Gyromitra esculenta* (n = 913) and *Corinarius rubellus* (n = 334). Most calls (85%) were from the public and 15% from healthcare professionals. Children under the age of six were involved in 60% (n = 6499) of enquiries and 74% of these concerned unidentified mushroom. In adults, the mushroom was identified in most cases and only 13% of the calls concerned unidentified mushrooms. Approximately 90% of the children under the age of six were considered asymptomatic at the time of the call. Most of the adults (70%) were symptomatic and 18 adults received MARS treatment. Eight (44%) of the MARS-treated patients were originally from Southeast Asia. One of the MARS-treated patients had to undergo liver transplantation. All the MARS-treated patients recovered. There was one lethal case involving a 77-year-old Finnish woman with suspected unconfirmed *Amanita virosa* poisoning.
Conclusion: The number of mushroom poisonings in Finland is challenging to estimate. The number of enquiries received by FPIC is not comparative to the actual number of mushroom poisonings in Finland. Immigrants have a relatively high risk for severe mushroom poisoning. Fatal mushroom poisoning is rare in Finland.

113. Outcome of comatose individuals found in a public space but were not intubated despite a Glasgow Coma Score of eight or less

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Objective: It is unknown whether intoxicated patients benefit from intubation for airway protection. Many clinicians intubate patients with a Glasgow Coma Score (GCS) of eight or less. These criteria for intubation were validated in head trauma patients and may not necessarily apply to intoxicated patients. Here, we describe the outcome of a series of intoxicated patients who were not intubated despite having a GCS of eight or less.
Methods: The study was designed as a retrospective chart review. In total 568 patients out of 1558 admissions for acute intoxication to our institution between 1 January 2016 and 31 December 2017 were found helpless in a public space. Complete toxicology screens were performed in 255 patients and of these patients, 53 had a GCS of eight or less.
Results: Of the 53 patients only 8 were intubated according to general practice, whereas 45 patients were not intubated. All patients survived. Aspiration pneumonitis was diagnosed in 2/45 non-intubated patients and in 2/8 intubated patients. Naloxone was used in 13 cases while flumazenil was used thrice. Most (34/45) patients had taken a mixture of medications/drugs, five had only consumed alcohol, one took antidepressants and five a single illegal drug. The following substances were detected: alcohol (n = 27), tetrahydrocannabinol (THC) (n = 18), opiates (n = 14), benzodiazepines (n = 27), synthetic cannabinoids (n = 2), pregabalin (n = 22), amphetamines (n = 6), buprenorphine (n =7), and methadone (n = 6).

Conclusion: The majority of comatose acutely intoxicated patients found in a public space could be managed safely without endotracheal intubation. These data cast doubt on strategies that use classical head trauma criteria for endotracheal intubation in this subgroup of acutely intoxicated adults. However, these data may not apply to other subgroups, such as patients with overdoses of therapeutic drugs.

114. Levocarnitine for acute valproic acid poisoning: our experience

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Objective: Valproic acid (VPA) is a fatty acid with anticonvulsant properties, well known for its widespread prescription and its implication in drug poisoning during suicide attempts. It is usually well tolerated in chronic treatment, but it may produce several side effects due to long-term administration including pancreatitis, hepatotoxicity, hyperammonemic encephalopathy, and bone marrow suppression [1]. The aim of our present study was to investigate the effect of levocarnitine supplementation on ammonemia and clinical recovery in patients with valproic acid-induced intoxication.
Methods: This study included all patients admitted for acute VPA poisoning (VPA >100 µg/mL), from 2014-2017, in our Intensive Care-Toxicology Unit of the Clinical Emergency Hospital, Bucharest, Romania. Blood samples were obtained to analyze ammonia and VPA concentrations and biochemical status. Consented subjects were then randomized through sealed envelopes with a concealed 1:1 allocation to either standard therapy (Group 1) or 1800 mg of L-carnitine/day together with standard therapy (Group 2) for 3 days.
Results: A total of 189 patients were enrolled in the study, 92 in Group 1 and 97 in Group 2, with no differences between the two groups according ingested dose, severity of symptoms, peak VPA concentration. There was a mean time elapsed between drug self-administration and hospital presentation of 3.2 ± 0.6 hours as reported by the patient or their relatives. Mean time to onset of encephalopathy symptoms was 6.8 ± 4.4 hours following the ingestion. The median (IQR) ingested dose of VPA was 1100 mg (820, 1200 mg [range; 800-6400 mg]). L-Carnitine supplementation resulted in significant reductions in ammonemia (44.8 ± 6 versus 66.2 ± 9.4 µmol/L), comparing 24 hour and baseline concentrations ($P < 0.001$). The trend was similar for plasma VPA concentrations ($p < 0.05$). Duration of hospitalization was shorter in Group 2 patients (7.8 versus 11.8 days, $p < 0.005$).
Conclusion: The use of L-carnitine accelerates the elimination of VPA and facilitates the decrease in ammonia plasma concentrations. We suggest that L-carnitine supplementation should be considered in the management of VPA intoxications in adults with hyperammonemia in order to reduce morbidity and mortality.

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115. The ICU Requirement Score (IRS) – does it identify poisoned patients who do not need intensive care unit referral? A validation cohort study

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Objective: The ICU requirement score (IRS) has been developed recently to identify poisoned patients who will not need intensive care (ICU) admission in an effort to minimize hospital expenses [1]. To date, this score has been poorly validated. We aimed to evaluate the IRS in a large cohort of intoxicated patients admitted to a French University Hospital ICU.
Methods: We performed a single-center retrospective cohort study. IRS was calculated using the clinical parameters obtained on admission: age, systolic blood pressure, heart rate, Glasgow Coma Score, intoxication type, co-morbidities (i.e., arrhythmia, cirrhosis and respiratory insufficiency), and combination of intoxication with another reason for ICU admission. We evaluated the ability on admission of IRS <6 to predict no need for ICU treatment defined as the need for mechanical ventilation, vasopressors, renal replacement therapy in the first 24 hours following admission and/or the onset of death during hospital stay. This score was compared to the usual scores (Simplified Acute Physiology Score (SAPS) II and III, Sequential Organ Failure Assessment (SOFA) score and Poison Severity Score).
Results: During the study period, 2514 poisoned patients were admitted, 1011 patients were excluded as requiring ICU treatment on admission and 1503 patients included in the study. Among the 1503 patients, 232 met the endpoint while only 23/510 patients (4.5%) with IRS <6 presented the endpoint and one patient died. The area under the curve of the ROC curve of the IRS was 0.736 (95% confidence interval (CI): 0.702–0.770). The negative predictive value of the IRS <6 was 95% (93-97), its sensitivity 89% (85-93), specificity 38% (36-41) and positive predictive value 21% (18-24). The performance of IRS was almost comparable to the other scores that are not readily available on hospital admission.
Conclusion: Our data demonstrate the excellent negative predictive value of the IRS, allowing excluding the transfer to ICU of patients with IRS <6. A prospective multicenter study is required to definitively confirm IRS usefulness.

Reference

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116. Massive gamma-hydroxybutyric acid overdose resulting in severe metabolic acidosis requiring continuous venovenous haemofiltration

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Objective: Severe metabolic acidosis from gamma-hydroxybutyric acid (GHB) overdose is rare. We describe a case requiring dialysis and the associated GHB concentrations.
Case report: A 31-year-old male, presented to the hospital emergency department via ambulance half an hour after taking 250 mL of GHB with suicidal intent. On arrival to the emergency department, he showed signs of gross psychomotor agitation requiring physical and pharmacological restraint with intramuscular midazolam and droperidol. An initial blood gas showed pH 7.24, bicarbonate 20 mmol/L, pCO_2 46 mmHg and lactate 4.4 mmol/L. He became sedated and over subsequent hours had several periods of apnoea and was intubated. He was persistently hypotensive requiring treatment with a noradrenaline infusion. In the intensive care unit (ICU) his blood gases were pH 6.81, bicarbonate 8 mmol/L, pCO_2 51 mmHg and lactate 2.9 mmol/L. Continuous venovenous haemodiafiltration (CVVHDF) was commenced at 12 hours post-ingestion and continued for 9 hours. The blood GHB concentration at 9 hours post-ingestion prior to CVVHDF was 2300 mg/L. The extraction ratio of GHB at 17 hours post-ingestion was 46% with a plasma clearance of 54.3 mL/min on CVVHDF (blood flow rate and ultrafiltration rate 200 mL/min). The apparent half-life of GHB whilst on CVVHDF was 3.5 hours compared to 5 hours after it was ceased. His acid-base status improved and he was extubated on day 2 of his ICU admission. He was discharged to the inpatient psychiatric unit under a treatment order on day 3.
Conclusion: GHB has a low molecular weight, small volume of distribution and minimal protein binding. This coupled with the ability to achieve clearance during dialysis of GHB may make this a reasonable treatment option in massive overdose and may decrease length of hospital stay and morbidity. Massive GHB overdose can result in severe metabolic acidosis. Dialysis with CVVHDF can assist with removing GHB and correcting the acid-base disturbance.

117. Hyperemesis and acute kidney injury following a "rebirth" ceremony with kambô and iboga in the Netherlands

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Objective: Kambô is a traditional healing ritual performed in many South American countries, with the purpose of purifying the body and mind of negative energy. It involves application of a poisonous mixture secreted from a frog, *Phyllomedusa bicolor*, consisting of several bioactive peptides. Within minutes of applying the secretion into burn wounds, people experience extreme nausea and start vomiting. Despite the lack of scientific data on the effects and toxicity of kambô, it is becoming increasingly popular in Europe. Ibogaine is an indole alkaloid isolated from the roots of the West African shrub *Tabernanthe iboga*. Besides its hallucinogenic effects, it has the ability to reduce withdrawal symptoms and drug-craving and has been used to help opioid dependent patients. Its action is complex, involving several different neurotransmitters. The adverse effects described are nausea, vomiting, ataxia and arrhythmia (QT prolongation). We describe a case of hyperemesis and acute kidney injury in a patient following a kambô and iboga ritual in the Netherlands.
Case report: A 30-year-old Belgian man, a known cocaine and cannabis user, was admitted to the intensive care unit because of persistent vomiting without diarrhea. He was sweaty and shivering, looked pale and gave a very ill impression overall. No neurological or cardiovascular abnormalities were observed. Several burn marks were visible on his left upper arm. Three days earlier the patient had travelled to the Netherlands to undergo a "rebirth" ceremony. The ritual started with kambô where a shaman applied the skin secretion of the frog, *Phyllomedusa bicolor,* into freshly burned skin. Thereafter, he ingested three capsules containing ibogaine and started vomiting until hospitalization. Laboratory results revealed a leukocytosis, acute kidney injury, rhabdomyolysis and metabolic alkalosis. Subsequent toxicological analysis by gas chromatography-mass spectrometry confirmed ibogaine in urine. In addition, metabolites of cannabis and cocaine were also detected. The patient recovered completely after receiving intravenous fluid, dexamethasone and ondansetron. He was discharged after 2 days.
Conclusion: Since little is understood about appropriate dosage, the administration of ibogaine comes with serious risks including sudden death. Although illegal, kambô and iboga are very popular among drug addicts, so more medical emergencies are expected. In case of extreme vomiting and QT prolongation among drug abusers, a general toxicological screen is recommended to detect possible ibogaine abuse.

118. Drug abuse trends, focussing on novel psychoactive substances (NPS) over the last three years (2016-2018) from the perspective of the Austrian Poisons Information Centre

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Objective: In recent years increasing numbers of new psychoactive substances (NPS) have appeared on the market. The purpose of this study was a trend analysis of the last three years from the perspective of the poisons information centre (PIC).
Methods: A retrospective review of enquiries to the PIC concerning drug ingestions in the last three years was performed. The extracted data included the most common NPS, caller (hospital, ambulance or private citizens), Poisoning Severity Score (PSS) and age.
Results: In total 596 cases regarding drug abuse were extracted from the database. There were 300 mono- and 296 combined intoxications (more than one substance, drugs mixed with medicines or with alcohol). In 58 cases, NPS were involved: 36 in mono- and 22 in combined intoxications. There were 44 enquiries regarding adults (18-45 years), 10 adolescents (14-17 years) and the age of 4 people was unknown. The most common substance groups of NPS were: synthetic cathinones (n = 18), synthetic cannabinoids (n = 11), opioids (n = 10), phenethylamines: (n = 7), amphetamines: (n = 3), other stimulants (n = 7), arylcyclohexylamines (n = 3), LSD-analogues (n = 1) and tryptamines (n = 2). The PIC was contacted by hospitals in 42 cases, by the emergency medical service in nine cases and in seven cases by lay persons. At the time of PIC consultation 37 patients (64%) had mild (PSS1), nine patients (16%) moderate (PSS2), four patients (7%) severe symptoms (PSS3), six patients (10%) were asymptomatic and in two cases (3%) the condition of the patient was unknown. There were two fatal cases. Case 1: a 25-year-old man

ingested an unknown amount of three NPS: BUC-8 (buprenorphine-analogue), 2-FMA (2-fluoromethamphetamine) and NEH (N-ethyl-hexedrone). At the time of the first contact the patient was already in the intensive care unit and had severe symptoms: coma (Glasgow Coma Score (GCS) 2-3), metabolic acidosis, tachycardia and hypoxia. The computerised tomography scan showed multiple small brain infarcts. He died after two days. Case 2: a 30-year-old man had a cardiac arrest soon after ingestion of the synthetic opioid U-47700. After resuscitation he was comatose (GCS 3), intubated and had miosis. Despite administration of naloxone and reanimation his condition deteriorated and he died after two days.
Conclusion: In our evaluation most patients had symptoms. Medical observation has to be recommended in these cases because the course of poisoning is often unpredictable. New opioids in particular present a high risk of lethality. In order to obtain a better control of the drug market, intensive cooperation of all involved institutions is needed.

119. 3,4-Methylenedioxy-α-pyrrolidinohexiophenone (MDPHP): four severe confirmed intoxications

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Objective: 3,4-Methylenedioxy-α-pyrrolidinohexiophenone (MDPHP) is a cathinone derivative developed in the 1960s, which recently appeared on the drug market. Human toxicological data are rare [1–3] and we describe four confirmed cases.
Case series: An observational case series of four intoxications treated in the Emergency Department at the University Medical Centre in April and May 2019. Medical history could not be obtained initially. After immunological pretesting of urine samples toxicological analyses using gas chromatography-mass spectrometry (GC/MS) were performed. Medical records were reviewed to obtain clinical data.
Clinical effects of stimulants comprising agitation, aggression, arterial hypertension and psychosis were recorded. In all cases, MDPHP and metabolites were detected in the urine, in one case with α-pyrrolidinovalerophenone (α-PVP). Serum concentrations were determined by liquid chromatography-mass spectrometry (LC-MS) and were 38, 16, 33 and 18 ng/mL. In three cases methadone was found (maintenance treatment) and in two cases morphine, with acetylmorphine, codeine and meconine in one patient. Two patients had significant QT-prolongation (QTc 616 ms and 471 ms, respectively) and two patients had elevated creatine kinase (1416 [CKMB 75 U/L (<25U/L)] and 1468 U/L [30-200 U/L], respectively). In three patients the C-reactive protein was significantly elevated (70.6, 10.1, 17.6 mg/L [<5 mg/L]). In addition to these four cases MDPHP was also detected in 10 routine samples. In these cases the medical history was not available.
Conclusion: In four cases of severe intoxication, which required emergency treatment, MDPHP was verified using GC-MS. The screening tests applied did not detect cathinone derivatives. All patients had a history of multiple drug abuse and a reduced general state of health. The detection of MDPHP in several routine samples may suggest more frequent MDPHP consumption in subtoxic doses. In cases of intoxication without a medical history, or in cases of opioid history and multi drug use detailed toxicological analysis may reveal new psychoactive substances which are not detected by standard toxicological screening approaches. The noticeable ECG changes seen in patients with MDPHP use need attention and confirmation.

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120. Presentations related to novel psychoactive substance use at three urban emergency departments in Switzerland

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Objective: Novel psychoactive substances (NPS) have emerged in recent years in response to market trends and legislative control. There are currently limited data on acute medical problems and patient characteristics related to recreational NPS use in Switzerland.
Methods: Retrospective analysis within the European Drug Emergencies Network (Euro-DEN) Plus project of cases presenting with acute toxicity related to recreational use of NPS at three emergency departments in Switzerland: the University Hospital of Bern (May 2012 – July 2019), the University Hospital of Basel (October 2013 – June 2019) and the Ente Ospedaliero Cantonale of Southern Switzerland (October 2016 – June 2019).
Results: During the study period, there were 16 cases related to acute toxicity of NPS (8 cases in Bern, 8 cases in Basel and no cases in Southern Switzerland). The mean patient age was 29 years (SD 10.8) and 75% (n = 12) were male. Case characteristics are shown in Table 1.
Conclusion: Emergency department presentations related to acute NPS toxicity appear to be rare in Switzerland. Most patients were young and male; the most frequently involved NPS were from the 2C-series and most intoxications of minor or moderate severity. The discrepancy between the reported and analytical results in some cases might be due to analytical limitations (e.g. NPS cannot be detected with the commonly used immunoassays), but might also indicate that some patients are unwilling to

Table 1. Case characteristics of patients presenting with novel psychoactive substance use in Switzerland.

Case	Sex	Age (years)	Substance (s) (reported)	Alcohol co-ingestion reported	Lowest GCS	Main Symptoms	Severity (assessed with [1])	Analytical results	Treatment	Outcome
1	F	32	**MDMC (methylone)**	yes	alert	Vomiting, palpitations, anxiety, agitation, tremor, muscle spasms, sweating, paresthesias, dizziness, agitation	moderate	IA: negative	Sedation (lorazepam), metoclopramide, i.v. fluid administration	Discharged home the same day
2	M	19	**2C-B**	yes	alert	Hallucinations, tachycardia, anxiety, agitation, mydriasis, confusion	moderate	LC-MS/MS: **2C-P**	Sedation (benzodiazepines, haloperidol)	Discharged home 11 h later
3	F	25	**2C-B**, amphetamine	N/A	15	Muscle spasms, anxiety	minor	IA: amphetamine, benzodiazepines (iatrogenic)	Sedation (midazolam), i.v. fluid administration	Discharged home
4	M	16	N/A	N/A	3	Hypotension, tachycardia, hypopnea, cyanosis, anxiety	severe	IA: negative, LC-MS/MS: **carfentanyl**	Intubation, naloxone, flumazenil	Discharged home the following day
5	M	18	**4-AcO-DMT**	N/A	10	Agitation, mydriasis	moderate	IA: benzodiazepines (iatrogenic)	Sedation (midazolam), i.v. fluid administration	Discharged home
6	F	21	**2C-B**	N/A	15	Palpitations, anxiety	minor	N/A	Sedation (lorazepam)	Discharged home
7	M	28	**3-MMC**, crystal meth	No	15	Panic attack, palpitations, dyspnea	moderate	N/A	N/A	Admission to psychiatric clinic
8	M	26	**2C-B**, cocaine	Yes	15	Palpitations, hallucinations, agitation, sweating	minor	IA: methamphetamine, cocaine	i.v. fluid administration	Discharged home
9	M	29	MDMA	Yes	Alert	Hallucinations, chest pain, palpitations, dyspnea, mydriasis	moderate	IA: negative, LC-MS/MS: **2C-B**	N/A	Discharged home
10	M	24	Amphetamine, MDMA, cannabis, cocaine	Yes	Alert	Psychosis, aggression	minor	LC-MS/MS: **mephedrone,** MDMA, amphetamine	Sedation	Discharged home
11	M	36	**Designer drug from internet**	No	5	Somnolence	moderate	IA: Benzodiazepine, cannabis, buprenorphine LC-MS/MS: morphine, temazepam	N/A	Admission to intensive care
12	M	49	**Fentanyl-like substance from Darknet**	No	3	Bradycardia, bradypnoea, coma	moderate	N/A	N/A	Discharged home
13	M	30	**2C-B**	N/A	Alert	Anxiety, fear that he would forget to breath	moderate	IA: negative	Sedation	Discharged home
14	F	53	Tramadol	N/A	14	Agitation, delusional parasitosis, hallucinations, psychosis	moderate	LC-MS/MS: **pentylone,** tramadol	Sedation	Admission to psychiatric clinic
15	M	42	Superman-XTC (MDMA and **PMMA**), methadone, benzodiazepine	N/A	3	Hypertension, coma	severe	IA: cannabis, opiates, benzodiazepins, LC-MS/MS: negative for NPS	Intubation, sedation, naloxone, flumazenil	Admission to intensive care unit
16	M	22	**2C-P**	yes	14	Dizziness	minor	N/A	N/A	Discharged home

F: female; M: male; GCS = Glasgow Coma scale; IA: Immunoassay; LC-MS/MS: liquid chromatography coupled with mass spectrometry; N/A = not available; h: hours; i.v.: intravenous; 2C-B: 2,5-dimethoxy-4-bromophenethylamine; 2C-P: 2,5-dimethoxy-4(n)-propylphenethylamine; 3-MMC: 3-methylmethcathinone; 4-AcO-DMT: O-Acetylpsilocin; MDMC: 3,4-methylenedioxymethylcathinone; PMMA: paramethoxymethamphetamine.

report the NPS intake or are unaware of the exact substance used.

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121. MDMA-related presentations to the emergency departments of the European Drug Emergencies Network (Euro–DEN) over the four-year period 2014-2017

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Objective: 3,4-Methylenedioxymethamphetamine (MDMA) remains one of the most commonly used recreational drugs and there has been an increase in the availability of higher strength MDMA in Europe recently. Monitoring of Emergency Department (ED) presentations with acute toxicity associated with MDMA is important to determine trends in MDMA use and harms.
Methods: Data were extracted from the European Drug Emergencies Network (Euro-DEN) Plus database for all ED presentations with acute toxicity involving MDMA use, alone or in combination with other substances, between 2014 and 2017. Frequency, geographical distribution, temporal trends, patient demographics, initial observations and clinical features, management, and outcome were analysed.
Results: Over the 4-year period, 2013 (8.4%) of the 23,947 Euro-DEN Plus presentations involved MDMA, used alone (88, 4.4%) or with other substances (1925, 95.6%). MDMA-related presentations peaked in 2016 (10.3% of the presentations in 2016 versus 8.3% in 2015, $P = 0.0005$), subsequently decreasing in 2017 (7.4%, $P < 0.0001$). The proportion of MDMA-related presentations varied by centre from over 15% (Slovakia 15.6% and Czech Republic 15.4%) to less than 2% (Lithuania 1.6% and Latvia 1.2%). Most presentations were in males (1436, 71.3%). Median age (23 years among females and 25 years among males) overall increased from 24.0 years (interquartile range, IQR, 20.0-27) in 2014 to 25.0 years (IQR 21.0-30.0) in 2017 ($P = 0.004$). From 2014 to 2015 there was an age-shift from individuals <35 years (91.9% in 2014 versus 86.6% in 2015) to ≥35 years (8.1% in 2014 versus 13.4% in 2015; $P = 0.02$). Compared to presentations of acute toxicity with other substances, MDMA-related presentations occurred more frequently during the weekend (61.5% versus 42.8%, $P < 0.0001$), and at night (between 8pm and 8am, 64.3% versus 53.2%, $P < 0.0001$). MDMA-related presentations more frequently had tachycardia (53.6% versus 29.2%, $P < 0.0001$), agitation (58.6% versus 40.4%, $P < 0.0001$), received sedation (57.9% versus 37.6%, $P < 0.0001$), and were medically discharged (62.4% versus 58.2%, $P = 0.0004$).
Conclusion: This large multicentre series of MDMA-related ED presentations showed geographical variation and changes over time in the demographics and proportion of presentations relating to acute MDMA toxicity. MDMA is commonly used with other substances, with acute toxicity presentations more common over the weekend and at night. MDMA toxicity was associated with sympathomimetic effects requiring sedation more frequently than acute toxicity with other substances. Triangulation of this with data from complementary sources including seizures, purity, prevalence of use, of deaths and wastewater analyses will enable a greater understanding of the public health implications of MDMA use in Europe.

122. A retrospective study of observation times in a healthcare facility and 48-hour mortality after heroin overdose with naloxone rescue

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Objective: Observation times following heroin overdose rescued with naloxone therapy remains highly variable among healthcare practitioners. Current expert opinion often recommends that patients be observed for 4-6 hours for respiratory depression and encephalopathy. Recent studies published in the last year have debated whether patients with return to baseline mentation and normal vital signs require such prolonged monitoring. The primary goal of this study is to report on observation times after naloxone administration in patients with reversal of the opiate toxidrome following heroin use and to determine if any subjects died within 48 hours of being discharged from the emergency department (ED).
Methods: In this retrospective observational study, the electronic medical records at a tertiary healthcare emergency department were queried from January 2017 through June 2018 for diagnosis codes linked to heroin and opiate toxicity. Included subjects were older than 17 years with suspected heroin intoxication who sustained improvement following naloxone rescue therapy either by pre-hospital providers or when given immediately upon arrival

to the ED. Subjects were excluded if they had ingested substances other than heroin, were admitted to the hospital for a non-overdose related pathology, did not return to cognitive baseline following naloxone therapy, or lived in a county other than our healthcare facility. Subjects were compared with the county Coroner/Medical Examiner office data which collects mortality information on all residents in the county to ensure that no subjects expired within 48 hours of being discharged from the ED. Demographics, duration of observation, need for additional doses of naloxone, and vitals following rescue therapy were all recorded. This study was approved by our institutional review board.

Results: Of the 105 subjects that met the inclusion criteria, 70 (66.7%) were male and 74 (70.5%) were between 26 and 45 years old. Fourteen (13%) required additional doses of naloxone in the ED. Of these 14 subjects, 6 were re-dosed for encephalopathy, 4 for rebound respiratory depression, 2 for both encephalopathy and respiratory depression, and 2 subjects received naloxone for unknown reasons. The mean observation time in the ED was 279 minutes (SD: 717 minutes); 38 subjects (36.2%) were observed less than 4 hours. No subjects died within 48 hours.

Conclusion: In our study, many subjects with naloxone rescue following heroin overdose were observed for less than 4 hours. Despite these observations times, there were no deaths in our cohort at 48 hours.

123. Admission predictors for cocaine users

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Objective: Cocaine users present to the emergency department (ED) with a broad and heterogeneous symptomatology. Some of these disorders may require hospital admission [1]. The objective of this study was to analyse the parameters and the factors related to a higher probability of admission after cocaine use.

Methods: Retrospective descriptive study, carried out in a tertiary hospital ED, including ED presentations of cocaine users, 2011-2017. Variables: epidemiological, clinical presentation, ECG findings and treatment. A multivariate analysis was performed to assess their association with hospital admission. Chi-squared test was performed for categorical variables, together with Cramer's V test (Φ_c).

Results: A total of 13.6% (109/800) of patients were admitted (Table 1). The mean age of admitted patients was higher compared to those discharged from the ED ($p < 0.001$. Multiple substance exposure was not associated with higher admission rates (12.2%) when compared with cocaine use only (17.8%), except for cocaine and pharmaceuticals ($n = 37$, $p < 0.001$). Renal, digestive symptomatology or rhabdomyolysis were associated with admission ($p < 0.001$). ECG findings associated with admissions were ST abnormalities ($p < 0.001$) and ventricular arrhythmias ($p = 0.004$). The need for non-specific emergency supportive procedures (e.g. observation, monitoring and fluid therapy), coronarography and treatment with antiarrhythmics, were also positively associated with admission to the hospital ($p < 0.001$).

Conclusion: Admission rates for cocaine use were higher in our study when compared with previously published data (between 5-10%) [2]. Hospital admission was associated with a higher mean age, renal or digestive symptomatology, rhabdomyolysis, ST disorders or ventricular arrhythmias, and the need for therapeutic measures in the ED.

Table 1. Patient characteristics, symptoms and treatments in cocaine users, comparing those admitted and those discharged from the emergency department.

	Admission		Non-admission		
Parameter	N	(%)	N	(%)	P value
Total number of patients	109	13.62	691	86.37	
Male	89	81.65	510	73.8	0.093
Female	20	18.34	181	26.2	
Mean age (years)	38.8		35.03		<0.001
SD	9.877		9.923		
Only cocaine	29	26.6	128	18.5	0.059
Multiple substances	80	73.4	563	81.5	
Symptoms					
None	0	0	21	3.03	
Cardiovascular	20	18.34	124	17.94	0.987
Neurologic	54	49.54	291	42.11	0.176
Psychiatric	45	41.28	359	51.95	0.047
Traumatic	18	16.51	75	10.78	0.065
Renal	10	9.17	3	0.43	< 0.001
Respiratory	22	29.18	41	5.93	0.012
Digestive	3	2.75	71	10.27	< 0.001
Rhabdomyolysis	13	11.92	6	0.86	< 0.001
ECG findings					
Not performed	42	38.52	340	49.2	
Performed	67	61.48	351	50.8	0.058
Normal	29	43.28	172	49	0.398
Sinus tachycardia	23	34.32	146	41.59	0.366
SV arrhythmia	1	1.59	2	0.56	0.395
ST disorders	18	26.86	28	7.97	< 0.001
Ventricular arrhythmias	4	5.9	0	0	0.004
Other	9	13.43	17	4.84	0.01
Treatments					
None	17	15.59	208	30.1	0.002
Observation/monitoring	55	59.77	115	23.8	0.001
Fluid therapy	41	44.56	97	20.08	0.001
Antidotes	17	18.47	63	13.04	0.132
Physical restraint	9	9.78	77	15.94	0.157
Sedation	32	34.78	326	67.49	0.001
Antiarrhythmic	4	4.34	2	0.41	0.029
Beta-blockers	3	3.66	0	0	0.004
Coronarography	11	11.95	1	0.2	<0.001
Salicylate	8	8.69	1	0.2	<0.001
Other	70	76.08	95	19.66	

References

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124. In-patient prescription opioid detoxification: peculiarities of consumption and treatment outcomes

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Objective: Long-term use of prescription opioids causes physical dependence and addiction. For chronic pain patients hyperalgesia may also develop, which is a strong indicator for opioid detoxification [1]. Nevertheless, opioid usage is increasing and

problems associated it with continue to rise. We examine existing links between patients' gender, age, depression history, characteristics of prescription opioid consumption, and treatment outcomes.
Methods: A retrospective analysis of patient charts was conducted in the Toxicology Center of Vilnius University Emergency Hospital. Patients treated for prescription opioid addiction with the principle diagnosis of International Classification of Diseases (ICD-10) code F11.2 (Mental and behavioural disorders due to use of opioids) were included in the study. Patients, who had been hospitalized for reasons other than detoxification, or addicted to other psychoactive substances (except alcohol, nicotine and benzodiazepines), were excluded from the study. Data was analyzed via MS Excel and IBM SPSS 23.0 software, statistical significance was assumed when $p < 0.05$.
Results: In total, 42 patients hospitalized over the period 2011 to April 2019 were included in the study; there were 23 males (54.8%) and 19 females (45.2%). Average age was 57 ± 14.1 years. Eight different opioids were used by the patients. Eighteen patients (42.9%) used opioids for chronic cancer-induced pain relief and 24 (57.1%) for chronic pain not associated with cancer. A negative correlation between gender and depression was established ($\chi2 = 5.555$, rphi $= -0.364$, $p = 0.018$). Women of the study population were more prone to depression (31.6% versus 4.3%, $p = 0.018$). The average duration of opioid consumption was 60.8 ± 74.7 months (range 3 to 336 months). Morphine equivalent dose (ME) was significantly lessened during detoxification treatment: ME before treatment was 134.7 ± 128.2 mg and 4.7 ± 17.1 mg after. Most patients (85.7%, $n = 36$) successfully ceased opioid use during in-hospital treatment. For the remaining 6 patients, the ME was reduced and subsequent detoxification was recommended.
Conclusion: Less than 25% of patients suffered from depression, which was more prevalent in the women in this study population. The duration of opioid consumption varied from 3 to 336 months. Most patients successfully ceased opioid consumption following hospital treatment for detoxification.

Reference

[1] Baldini A, Von Korff M, Lin EH. A review of potential adverse effects of long-term opioid therapy: a practitioner's guide. Prim Care Companion CNS Disord. 2012;14.pii:PCC.11m01326.

125. In-patient prescription opioid detoxification: gender differences and harmful habits

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Objective: Long-term prescription opioid use frequently causes addiction, posing a risk of overdose and death. Nevertheless, their use is increasing [1] and few substitutes for treating chronic pain exist. A combination of opioids and benzodiazepines heightens the risk of overdose [2]. We examined differences between patients' gender, harmful habits, and their influence on morphine equivalent dose (ME) in patients treated at our center.
Methods: A retrospective analysis of patient charts was conducted at the Toxicology Center of Vilnius University Emergency Hospital. Patients treated for prescription opioid addiction with the principle diagnosis of International Classification of Diseases (ICD-10) code F11.2 (Mental and behavioural disorders due to use of opioids) were included in the study. Patients who had been hospitalized for reasons other than detoxification, or addicted to other psychoactive substances (except alcohol, nicotine and benzodiazepines), were excluded from the study. Data was analyzed via MS Excel and IBM SPSS 23.0 software, statistical significance was assumed when $p < 0.05$.
Results: Overall, 42 patients hospitalized over the period 2011 to April 2019 were included in the study; there were 23 males (54.8%) and 19 females (45.2%), with average age 57 ± 14.1 years. Nine (21.4%) were smokers (88.9% male). A positive correlation was established between smoking and gender ($\chi2 = 5.035$, rphi $= 0.350$, $p = 0.025$). Male smokers were significantly more common than women ($n = 8$, 34.8% versus $n = 1$, 5.3%, $p = 0.025$). Six patients (14.3%) admitted to using alcohol and a positive correlation was found ($\chi2 = 5.738$, rphi $= 0.371$, $p = 0.016$). Men were more prone to using alcohol ($n = 6$, 14.2% ir $n = 0$, $p = 0.016$). Fifteen patients (35.7%) used benzodiazepines (66.7% of them female). A negative correlation was established ($\chi2 = 4.325$, rphi $= -0.321$, $p = 0.038$). It was statistically significantly more common for women to use benzodiazepines ($n = 10$, 52.6% versus $n = 5$, 21.7%, $p = 0.038$). Average morphine equivalent dose (ME) at arrival was 137.7 ± 128.2 mg (range 20-690 mg). ME did not significantly differ between genders ($p = 0.107$). Smokers' ME was significantly higher than that of non-smokers (249.0 ± 232.2 mg versus 112.8 ± 91.8 mg, $p = 0.016$). Alcohol or benzodiazepines did not influence ME.
Conclusion: There were more smokers and alcohol drinkers among men, and women were more likely to consume benzodiazepines. Smokers had used higher doses of opioids, whereas alcohol or benzodiazepine use did not influence opioid dosage in this study.

References

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[2] Kim HS, McCarthy DM, Courtney DM, et al. Benzodiazepine-opioid co-prescribing in a national probability sample of ED encounters. Am J Emerg Med. 2017;35:458–464.

126. Clinical effects following the use of freely available herbal drugs: the toxicity of "Happy Caps"

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Objective: "Happy Caps" are commercially available herbal formulas with mood-enhancing effects. In addition to caffeine or caffeine-like substances (e.g. guarana, theobromine), some Happy Caps are claimed to contain an extract of Hawaiian baby woodrose seeds (HBW, *Argyreia nervosa*). These seeds contain a high percentage of the psychoactive substance lysergic acid amide (LSA), a natural analog of lysergic acid diethylamide (LSD). This study aimed to investigate the number of Happy Caps exposures reported to the Dutch Poisons Information Center (DPIC) and the clinical effects associated with exposure.
Methods: We performed a three-year prospective follow-up study (2016–2018) on Happy Caps exposures reported to the DPIC. Cases were followed-up by telephone with the patient and/or physician, using standardized questionnaires. Severity of symptoms was scored using the Poisoning Severity Score.

Results: We included 26 cases: 3 in 2016, 10 in 2017, and 13 in 2018. The patients' median age was 26 years (range 14-58 years; 58% male). Most products were bought in a smart shop (62%, n = 16) or online (12%, n = 3). The median ingested dose was 3 capsules (range 1–11 capsules). Most patients used Happy Caps labelled as containing HBW (85%, n = 22). Five patients (19%) had concomitant exposures to other drugs of abuse. Eight patients (31%) experienced mild symptoms, while 18 (n = 69%) developed moderate symptoms. These involved psychoactive effects only, such as hallucinations (69%, n = 18), anxiety (54%, n = 14), and confusion (35%, n = 9). All other (somatic) symptoms were mild. The onset of symptoms was usually within 3.5 hours after exposure (range 0.25-12 hours). Psychoactive effects were reported exclusively following ingestion of Happy Caps labelled as containing HBW. Mild cardiovascular symptoms were reported, including tachycardia (46%, n = 12), hypertension (23%, n = 6) and palpitations (23%, n = 6). Other reported symptoms were dizziness (46%, n = 12), gastrointestinal distress (42%, n = 11), and perspiration (38%, n = 10). Seven patients (27%) were monitored for several hours, but medical treatment was not required.
Conclusion: Exposure to Happy Caps, especially to those labelled as containing an extract of HBW seeds, frequently results in psychoactive effects classifying as a moderate intoxication. However, apart from these psychoactive effects, all intoxications were classified as mild. Severe toxicity was not reported, even at high doses (11 capsules). Product analysis could potentially clarify whether the psychoactive properties of Happy Caps are indeed due to the presence of herbal ingredients.

127. Analysis of Twitter content to explore use of modafinil and methylphenidate as drugs to facilitate studying in the UK

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Objective: Analysis of Twitter content has previously been used to monitor prescription stimulant use by college students in the United States [1]; however, there is no comparable published data from the UK. The aim of this study was to contextualise UK online discussion around use of modafinil and methylphenidate in relation to facilitating studying.
Methods: The RADARS® System Web Monitoring Program collects and organises online discussion concerning prescription drugs from a wide range of worldwide websites. For this study, Twitter posts originating from the UK mentioning modafinil, methylphenidate and/or their brand names between 1 October and 31 December 2018 were analysed. Duplicate tweets and posts relating to pop culture, online pharmacy, news stories and/or research studies with no other theme(s) present were excluded. Posts were searched for a total of 42 keywords (Table 1) and all posts containing one or more keyword were manually reviewed to identify those specifically discussing modafinil/methylphenidate use in relation to studying.
Results: One or more keywords were found in 74 of the total modafinil tweets (37.8%, n = 196) and 74 methylphenidate tweets (17.0%, n = 436). For modafinil the most common keywords were *"cognitive"* (n = 15, 7.7% of total modafinil tweets), *"smart"* (11, 5.6%), and *"nootropic"*, *"student"*, and *"study"* (each 10, 5.1%). For methylphenidate the most common keywords were *"school"* (n = 19, 4.4% of total methylphenidate tweets), *"focus"* (n = 15, 3.4%), *"brain"* (n = 11, 2.5%), and *"concentrate"* (n = 7, 1.6%). For modafinil 15.7% (n = 31) of posts discussed use as a study drug compared to only 3.7% (n = 16) of posts for methylphenidate.
Conclusion: Twitter posts confirm UK-based discussions about the use of methylphenidate and particularly modafinil to facilitate academic study and may contribute to normalising their use by students.

Table 1. List of keywords searched within Twitter posts relating to use of methylphenidate or modafinil to facilitate studying.

STUDY RELATED KEYWORDS			
Alevel	Alevel, A Level, 'A' Level, Alevels, A Levels, 'A' Levels	**Lecture**	Lecture, Lectures, Lecturer
Allnight	Allnight, All Night, All-night, Allnite, All Nite, All-nite, Allnighter, All Nighter, All-nighter, Allniter, All Niter, All-niter	**Lesson**	Lesson, Lessons
Assignment	Assignment, Assignments	**Library**	Library
Brain	Brain, Brainier	**Memory**	Memory
Campus	Campus, Campuses	**Midterm**	Midterms
Class	Class, Classes, Classroom	**Mock**	Mock, Mocks
Cognitive	Cognitive	**Nootropic**	Nootropic, Nootropics
College	College, Colleges	**Performance**	Performance
Concentrate	Concentrate, Concentrating, Concentration	**Productive**	Productive, Productivity
Cram	Cram, Crams	**Project**	Project, Projects
Degree	Degree	**Quiz**	Quiz, Quizs, Quizzes
Dissertation	Dissertation, Dissertations	**Report**	Report, Reports
Enhance	Enhance, Enhances, Enhancer, Enhancement, Enhancing	**Revise**	Revise, Revises, Revision
Essay	Essay, Essays	**School**	School, Schools
Exam	Exam, Exams, Examination	**Semester**	Semester, Semesters
Finals	Finals	**Smart**	Smart, Smarter, Smartdrug, Smartdrugs
Focus	Focus, Focused, Focusing	**Student**	Student, Students
GCSE	GCSE, GCSEs	**Study**	Study, Studys, Studying, Studied, Studies, Studious
Graduate	Graduate, Graduates, Graduation	**Test**	Test, Tests
Homework	Homework	**Thesis**	Thesis
Intellect	Intellect, Intellectual	**University**	University, Universities, Uni

Reference

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128. Non-medical use of prescription and over the counter opioids in the UK

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Objective: Non-medical use (NMU) of prescription opioids in the US is well documented and associated with significant morbidity and mortality, and it is a common reason for calls to poison centres and emergency department presentation. There is limited published data on the prevalence of opioid NMU in the UK.
Methods: Data from the UK online Survey of Non-Medical Use of Prescription Drugs (launched fourth quarter of 2018) were analysed [1]. Post-stratification weights were applied to responses from 9,926 individuals to represent the 53,370,283 adults living in the UK. Prevalence estimates and 95% confidence intervals (CIs) of last 12-month NMU were calculated, separately and combined, for any weak prescription opioid, any strong prescription opioid, and any over the counter opioid (Table 1) overall and for each region.
Results: Overall UK prevalence of last 12-month NMU of any opioid was 11.0% (95% CI 10.4-11.6) corresponding to approximately 5.9 million UK adults. The highest NMU prevalence was prescription codeine (5.3%, 4.9-5.8) followed by OTC codeine (4.5%, 4.1-4.9), tramadol (1.7%, 1.5-1.9), morphine (1.0%, 0.8-1.1), OTC dihydrocodeine (0.7%, 0.6-0.9) and prescription dihydrocodeine (0.6%, 0.5-0.8). Prevalence of NMU of all other prescription opioids was <0.5%. The highest NMU prevalence was seen in London, except NMU of any weak opioid which was highest in Northern Ireland. The biggest regional difference was for any strong prescription opioid: last 12-month NMU approximately six-times greater in London than the rest of England.
Conclusion: There is significant NMU of opioids in the UK with regional variation, particularly for strong prescription opioids. Further research is required to investigate factors responsible for the regional variation and determine motivations for and sources of prescription opioid NMU to inform design of public health interventions.

Table 1. Prevalence of last 12-month non-medical use of prescription and over the counter (OTC) opioids in the UK.

	Prevalence (95% Confidence Interval)			
Region	Any Weak Prescription Opioid[a]	Any Strong Prescription Opioid[b]	Any OTC Opioid[c]	Any Opioid (Prescription + OTC)[d]
All UK	6.5 (6.0-7.0)	2.6 (2.3-2.9)	4.9 (4.5-5.4)	11.0 (10.4-11.6)
London	7.7 (6.4-9.1)	8.3 (7.1-9.7)	7.9 (6.5-9.5)	18.0 (16.1-20.2)
England (except London)	6.2 (5.7-6.8)	1.4 (1.2-1.7)	4.5 (4.0-5.0)	9.6 (8.9-10.3)
Northern Ireland	8.4 (5.3-13.3)	5.0 (2.9-8.4)	5.3 (3.0-9.3)	13.7 (9.7-19.0)
Scotland	5.6 (4.2-7.5)	2.3 (1.6-3.5)	4.9 (3.5-6.7)	10.4 (8.4-12.8)
Wales	7.3 (5.3-10.0)	3.2 (1.9-5.2)	3.8 (2.4-6.0)	11.2 (8.6-14.5)

[a]Any weak prescription opioid: codeine, dihydrocodeine, or tramadol.
[b]Any strong prescription opioid: buprenorphine, diamorphine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, pethidine, sufentanil, or tapentadol.
[c]Any OTC opioid: codeine or dihydrocodeine.
[d]Any opioid total: any prescription or OTC opioid.

Reference

[1] Ng FL, Rockhill K, Black J, et al. UK survey of non-medical use of prescription drugs (NMURx) as a valuable source of general population illicit drug use data. Postgrad Med J. 2018;94:627–633.

129. Alternative routes of administration for non-medical use of prescription opioids in the UK

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Objective: Non-medical use (NMU) of opioids is a global cause for concern. An important component of NMU is use of drugs by a different route than intended, for example inhaling (snorting/smoking) or injecting tablet preparations. We investigated drug administration by alternative routes among those reporting last 12-month NMU of prescription opioids.
Methods: Data from the UK online Survey of Non-Medical Use of Prescription Drugs (collected end of 2018) were analysed [1]. Prevalence and 95% confidence intervals (CIs) of last 12-month NMU for prescription opioid single ingredient tablets were calculated. Amongst those reporting last 12-month NMU, the proportion and 95% CI were calculated for NMU by the intended route (swallowed) or by an alternative route (inhaled or injected).
Results: The highest prevalence of NMU was observed for codeine (3.7%, 95% CI: 3.4-4.1) and tramadol (1.4%, 1.2-1.6); prevalence was £0.5% for all other drugs (Table 1). Swallowing was the most common route of NMU for all drugs. Inhalation or injection was more common for strong opioids (buprenorphine, fentanyl, methadone, morphine and oxycodone) than weak opioids (codeine, dihydrocodeine and tramadol). Approximately one in five reported NMU by inhalation for strong opioids. Fentanyl (28.1%, 16.0-44.6) and buprenorphine (19.8%, 10.6-33.9) were the drugs most commonly injected.
Conclusion: The most common route of use for NMU of tablet preparation opioids in the UK is by the intended route of use. However, injecting and inhaling these products are significant routes of administration particularly for NMU of strong opioids. This has important public health implications as injection of drugs is associated with serious additional risks including local and blood-borne infections and inadvertent overdose.

Table 1. Prevalence of last 12-month non-medical use for single ingredient prescription opioid tablets and weighted proportion estimates for intended route of administration (swallowed) and alternative (inhaled or injected) route of administration among respondents reporting last 12-month NMU of single ingredient prescription opioid tablets (respondents can report more than one route so proportions do not sum to 100%).

	a) Prevalence Last 12 Month NMU Weighted % (95% CI)	b) Route of Administration Weighted Proportion % (95% CI)		
		Swallowed	Inhaled	Injected
Buprenorphine	0.3 (0.2-0.4)	64.4 (47.4-78.5)	19.5 (10.1-34.4)	19.8 (10.6-33.9)
Codeine	3.7 (3.4-4.1)	87.7 (84.0-90.7)	3.3 (2.0-5.4)	1.2 (0.6-2.3)
Dihydrocodeine	0.5 (0.4-0.6)	87.5 (77.9-93.3)	11.5 (5.6-22.3)	8.6 (3.8-18.2)
Fentanyl	0.2 (0.2-0.3)	55.9 (37.8-72.5)	24.0 (12.6-41.0)	28.1 (16.0-44.6)
Methadone	0.3 (0.2-0.4)	52.9 (36.7-68.6)	16.4 (7.6-31.7)	14.0 (7.0-26.1)
Morphine	0.5 (0.4-0.6)	65.3 (51.8-76.7)	19.8 (11.8-31.3)	11.8 (6.4-20.7)
Oxycodone	0.2 (0.2-0.3)	65.4 (46.5-80.5)	19.3 (9.3-36.1)	15.9 (7.5-30.8)
Tramadol	1.4 (1.2-1.6)	88.5 (83.2-92.3)	5.6 (3.4-9.3)	6.3 (3.8-10.1)

Reference

[1] Ng FL, Rockhill K, Black J, et al. UK survey of non-medical use of prescription drugs (NMURx) as a valuable source of general population illicit drug use data. Postgrad Med J. 2018;94:627–633.

130. The association between the availability of over the counter codeine and the prevalence of non-medical use

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Objective: Codeine is the most commonly used opioid worldwide and is available on prescription throughout Europe and also over-the-counter (OTC) in the UK. The sale of OTC codeine products has been banned in France and Australia due to concerns about rising codeine-related deaths [1,2]. Codeine-related deaths and the number of people in treatment for codeine dependence in the UK has also increased [3]. A survey of UK-based general practitioners found that 50% of them thought requests for codeine medicines were increasing and 87% believed the potential to buy codeine from multiple sources added significantly to the potential for misuse [4]. We investigated the prevalence of codeine non-medical use (NMU) in Germany, Italy and the UK and whether availability of OTC codeine has an association with NMU of the drug.

Methods: Data collected in the online Survey of Non-Medical Use of Prescription Drugs (NMURx) [5], in surveys launched in the second half of 2017 from Germany (n = 15,051), Italy, (n = 10,019), and the UK (n = 10,019) were analysed. For each survey, the estimated prevalence and 95% confidence interval (CI) of respondents reporting NMU of prescription and/or OTC codeine within the last 12 months were calculated and compared.

Results: The prevalence of last 12 month NMU in the UK was 11.8% (95% CI: 11.2-12.5) for prescription codeine, 15.9% (15.2-16.7) for OTC codeine and 22.4% (21.5-23.3) for any codeine (prescription and/or OTC). The prevalence of last 12 month NMU for prescription codeine was 6.3% (5.9-6.7) in Germany and 6.3% (5.8-6.9) in Italy.

Conclusion: The prevalence of last 12 month NMU of any codeine product is over three times greater in the UK compared to Germany and Italy where the drug is only available by prescription. Whilst other factors may contribute, these findings suggest that availability of codeine OTC is associated with greater NMU.

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131. Recreational nitrous oxide use rises dramatically after change in EU legislation

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Objective: Nitrous oxide (N_2O) is used as an anaesthetic, as a whipping agent for cream, and in the automotive industry. Besides these intended uses it is also abused recreationally. Due to European legislative changes in 2016, N_2O was transferred from the Medicines Act to the Commodities Act in the Netherlands, making it easily and legally available. Since then recreational use increased, mirrored by a rise in public nuisance by discarded N_2O cartridges and balloons, overt sales and use in public spaces and even impaired driving under the influence of N_2O. In 2019, Dutch burn centers reported severe frost-bite injuries to the legs of recreational users by holding small cylinders (several liters) of N_2O between their thighs during inhalation. Additionally, neurologists reported severe neurological damage following N_2O abuse, including paraplegia, likely due to N_2O-induced vitamin-B12 deficiency. We studied the effect of the

changed legal status of N_2O on the inquiries reported to the Dutch Poisons Information Center (DPIC).
Methods: We retrospectively analysed the number of inquiries on N_2O abuse reported to the DPIC, the quantities used and the associated health effects from 2008-2019. Extreme use was defined as over 50 balloons in one session.
Results: The number of inquiries on N_2O increased after 2016, with a clear upsurge in 2019. We received around 5 inquiries/year before 2014, 13 in 2015, 23 in 2016, 48 in 2017, 54 in 2018, and 67 in the first half of 2019. All patients reported adverse health effects, such as nausea, vomiting, headache, dizziness, chest pain, visual impairment, confusion, anxiety and tingling sensations or numbness in the arms and/or legs. Only a minority of patients (approximately 15%) had concomitant exposures to other drugs of abuse. N_2O-abusers were mainly young adults up to 30 years of age. In the first half of 2019, 52% of the cases (35 out of 67) concerned chronic abuse or use of extreme quantities of N_2O. Twenty out of 67 patients (30%) reported tingling or numbness, which could indicate neurological damage. Additionally, use from small cylinders has increased (22% of inquiries in 2019, 9% in 2018).
Conclusion: The European change in legal status of N_2O has led to an increasing number of health incidents in the Netherlands. The DPIC reported these findings to the Dutch health authorities and currently (October 2019) the Ministry of Health is conducting a risk assessment procedure on N_2O that will lead to preventive measures.

132. Analysis of drugs in blood and urine samples from suspected spiked drink victims

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Objective: Patients regularly contact emergency medicine services concerned that they have been poisoned by others, most frequently in the form of spiked drinks. The aim of this study was to identify drugs in blood and urine samples from patients with suspected poisoning inflicted by others.
Methods: A prospective observational study. From September 2018 to May 2019 we collected blood and urine samples from patients 16 years or older who presented at the Oslo Accident and Emergency Outpatient Clinic within 48 hours of suspected poisoning inflicted by others. The samples were analyzed, looking for the most commonly used recreational drugs and for the drugs most often used in poisoning inflicted by others. We also registered age, gender, clinical features, and treatment. Victims of sexual assault were not included in this study.
Results: Over the 37 week period, 101 patients (2.7 per week) presented at the clinic with suspected poisoning inflicted by others. We collected 101 blood samples and 71 urine samples. There were 64 females (63%) and 37 males (37%). Median age was 24 years. In the blood samples we found ethanol in 65 cases (64%), tetrahydrocannabinol (THC) in 4 (4%), benzodiazepines in 4 (4%), lamotrigine in 2 (2%), cocaine in 2 (2%), amphetamine in 4 (4%), methylenedioxymethamphetamine (MDMA) in 3 (3%), and tramadol in 1 case (1%). In the urine samples we found ethanol in 52 (73%), cocaine in 5 (7%), opiates in 2 (3%), cannabis in 5 (7%), benzodiazepines in 1 (1%), MDMA in 3 (4%), amphetamine in 5 cases (7%). The most commonly reported clinical features were amnesia, nausea, dizziness and vomiting. Most patients (n = 62, 61%) did not require any treatment; 36 patients (36%) were kept for observation, 3 patients (3%) were in need of treatment beyond mere observation and one patient was sent to hospital. No patients died.
Conclusion: Every week patients presented with suspected poisoning inflicted by others. Cases involving women were more common. In two thirds of the urine samples ethanol was the only drug detected, but several other drugs also occurred. In one third of the cases, no drugs were detected.

133. Serotonin toxicity and/or opioid withdrawal after the first dose of naltrexone/bupropion: an observational study

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Objective: In 2014, the FDA approved naltrexone/bupropion, a combination of an antidepressant and an opioid antagonist, for chronic weight management. Concurrent use of antidepressants and opioids has caused drug interactions involving serotonin syndrome. The package insert clearly states the potential for drug interactions and the risk of experiencing opioid withdrawal while taking naltrexone/bupropion with concomitant opioid use; however, it does not mention the risk for serotonin syndrome. Our primary objective is to identify cases of serotonin toxicity and/or opioid withdrawal after initiation of naltrexone/bupropion. Our secondary objective is to assess which specific opioids are more likely to cause a drug interaction with naltrexone/bupropion.
Methods: We reviewed cases in the RADARS® database from January 2014 through December 2018. The cases must have taken their first dose of naltrexone/bupropion with concomitant use of an opioid and met the inclusion criteria. Cases were determined to involve serotonin toxicity and/or opioid withdrawal using Hunter's Serotonin Toxicity Criteria and the Clinical Opioid Withdrawal Scale. The primary outcome measures were total number of cases with at least a moderate outcome, total number of cases determined to experience serotonin toxicity and/or opioid withdrawal, and total number of cases to experience serotonin toxicity and/or withdrawal with at least a moderate outcome. The secondary outcome measures included the frequency of different opioids, benzodiazepine administration, and supportive care with either mechanical ventilation or intubation.
Results: Overall, 33 cases met inclusion criteria, and 23 cases contained medical outcome. The 23 cases followed to outcome included two major, 14 moderate, and seven minor effects. Sixteen out of 23 cases (70%) had at least a moderate outcome. Seventeen out of 23 cases (74.0%) experienced serotonin toxicity (4 cases) and/or withdrawal (19 cases). Overall, 13 out of 17 cases (76.5%) experienced serotonin toxicity and/or withdrawal and resulted in at least a moderate outcome. Tramadol was the most common opioid involved in patients who experienced serotonin toxicity and/or withdrawal (6/17; 35.5%) and the most common opioid involved in serotonin toxicity cases (2/4; 50%).
Conclusion: Naltrexone/bupropion taken within seven days of an opioid may indirectly enhance serotonergic activity, causing excess stimulation at the 5-HT_{1A} or 5-HT_{2A} receptors through various mechanisms. This study suggests occurrence of a drug interaction in the form of serotonin toxicity and/or opioid withdrawal

with at least a moderate outcome after the first dose of naltrexone/bupropion while on opioid therapy.

134. Gamma-hydroxybutyrate (GHB) poisoning in a primary care emergency setting

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Objective: We describe patients treated for gamma-hydroxybutyrate (GHB) poisoning in a primary care emergency setting, their clinical features, treatment and triage for hospital treatment.
Methods: We registered all patients presenting with acute recreational drug toxicity at the Oslo Accident and Emergency Outpatient Clinic (OAEOC) in Oslo, Norway, from October 2013 through September 2015. The OAEOC is a primary care emergency outpatient clinic with limited diagnostic resources, treating the majority of patients with acute recreational drug toxicity in Oslo. Eligible patients were retrospectively identified from the local electronic medical records. We did not register patients with sole alcohol intoxication, suicidal intent or poisoning inflicted by others. We registered age, gender, toxic agents taken, clinical features, treatment, disposition, and length of stay. For this study we extracted the cases involving GHB.
Results: GHB was involved in 329/3234 (10.2%) cases. Among these 329 cases, median age was 30 years and 101 (30.7%) were female. GHB was the only reported toxic agent in 128 cases (38.9%), combined with ethanol in 96 cases (29.2%), amphetamines in 65 (19.8%), benzodiazepines in 49 (14.9%), heroin in 46 (14.0%), cannabis in 14 (4.3%), and cocaine in 12 (3.6%). The most common clinical feature was reduced level of consciousness, 118 (68.5%) had a Glasgow Coma Score (GCS) < 15 and 43 (13.5%) were in a coma (GCS ≤7), while 117 patients (35.6%) were agitated. In cases where GHB was the only reported agent, the patient more often was agitated (43.0% versus 30.8%, $p = 0.034$). In 42 cases (12.8%) the patient was given treatment beyond mere observation while at the outpatient clinic. In 159 cases (48.3%) the patient was sent on to hospital. When GHB was the only reported agent, the patient was more frequently hospitalised (64.1% versus 38.3%, $p < 0.001$). Median length of stay at the outpatient clinic was 1:28 h. Length of stay was shorter for patients sent on to hospital (0:42 h [IQR 0:26 h to 1:23 h] versus 3:01 h [IQR 1:32 h to 4:42 h], $p < 0.001$). Patients sent on to hospital more often had a GCS ≤7 (23.3% versus 4.8%, $p < 0.001$) and were more often agitated (43.1% versus 28.4%, $p = 0.008$). No patients died at the outpatient clinic.
Conclusion: About half the patients with GHB poisoning were treated with limited diagnostic resources in a primary care setting. The half sent on to hospital had more severe symptoms and were quickly identified for hospitalisation.

135. Acute poisoning related to the recreational use of benzodiazepines

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Objective: We describe acute poisonings related to the recreational use of benzodiazepines.
Methods: Cases were included retrospectively from October 2013 through September 2015 at the Oslo Accident and Emergency Outpatient Clinic (OAEOC) in Oslo, Norway. The OAEOC is a primary care emergency outpatient clinic, treating the majority of patients with recreational drug toxicity in Oslo. We included all patients presenting with acute poisoning related to recreational drug use, except intoxications with alcohol only. We did not include suicide attempts or poisonings inflicted by others. We registered gender, age, drugs taken, clinical features, treatment, length of stay, and disposition from the OAEOC. For this study, we extracted the cases involving benzodiazepines (including Z-drugs).
Results: Benzodiazepines were involved in 1037/3234 (32.1%) cases. Among these 1037 cases, median age was 36 years (IQR 28–46), and 787 (75.9%) were male. Clonazepam was the most frequently occurring benzodiazepine (n = 575, 55.4%), followed by diazepam (n = 158, 15.2%), alprazolam (n = 125, 12.1%), oxazepam (n = 94, 9.1%), flunitrazepam (n = 31, 3.0%), zopiclone (n = 25, 2.4%), nitrazepam (n = 19, 1.8%), zolpidem (n = 11, 1.1%), flurazepam (n = 1, 0.1%), and unspecified benzodiazepines in 142 cases (13.7%). Benzodiazepines were the only drugs taken in 101 cases (9.7%). Benzodiazepines were combined with heroin in 484 cases (46.7%), ethanol (n = 321, 31.0%), amphetamine (n = 199, 19.2%), cannabis (n = 95, 9.2%), gamma-hydroxybutyrate (GHB) (n = 49, 4.7%), methadone (n = 45, 4.3%), buprenorphine (n = 34, 3.3%), cocaine (n = 32, 3.1%), methylenedioxymethamphetamine (MDMA) (n = 18, 1.7%), other opioids (n = 72, 6.9%), and other drugs in 23 cases (2.2%). Twenty-two patients (2.1%) were in a coma at presentation (Glasgow Coma Score (GCS) < 8), while 644 (62.2%) were somnolent (GCS score 8-14), and 111 (10.7%) had a respiratory rate <12/min. Apart from this, the most common clinical features were agitation (n = 150, 14.5%), and anxiety (n = 42, 4.1%). In 244 cases (23.5%) the patient was given treatment beyond mere observation. Naloxone was given in 187 cases (18.0%), sedation in 13 (1.3%), and flumazenil in 2 patients (0.2%). Median length of stay was 4:25 h (IQR 2:30 h to 6:11 h). In 188 cases (18.1%) the patient was sent on to hospital. No patients died at the OAEOC.
Conclusion: Benzodiazepines were involved in one out of three cases of acute recreational drug toxicity, most often in combination with opioids, ethanol and/or amphetamine. Two out of three patients were somnolent or comatose at presentation, and one out of five needed hospitalisation.

136. Treating patients with opioid overdose at a primary care emergency outpatient clinic: a cost-minimization analysis

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Objective: In Oslo, Norway, most patients with acute poisoning by substances of abuse are treated at a primary care emergency

facility. Our aim was to conduct an economic evaluation of this strategy against treatment in a hospital setting, which is the norm in most other places. Previous research has shown that the clinical outcomes of these strategies are nearly identical [1], implying that a cost-minimization analysis is appropriate.
Methods: A representative patient with opioid overdose was constructed based on the cohort of all patients treated for opioid overdose at the Oslo Accident and Emergency Outpatient Clinic (OAEOC) during one year (October 2011 through September 2012, n = 539). Patient information included age, gender, mode of presentation, toxic agents taken, clinical observations, complications, treatment, length of stay, and disposition. The expected resources used on this patient at the OAEOC was estimated based partly on data from the observed cohort and partly on discussions with experienced local clinicians. Information about the treatment in a hospital setting was obtained at Drammen Hospital, where discussions with experienced staff were used to estimate the expected resource use. The expected costs were then calculated at both places.
Results: The estimated expected per patient cost at OAEOC was 153 EUR (1 EUR =7.57 NOK), comprising personnel costs of 123 EUR and treatment costs of 30 EUR. The corresponding cost at Drammen Hospital was 770 EUR, comprising personnel costs of 234 EUR, treatment costs of 230 EUR, and costs associated with admission to the intensive care unit of 305 EUR. The point estimate of the cost difference was 617 EUR per patient, with a low-difference scenario and high-difference scenario estimated at 292 EUR and 977 EUR, respectively.
Conclusion: Treating patients with opioid overdose at a primary care emergency facility is highly cost-effective, compared to treating them in a hospital setting. The results are most likely transferable to poisonings with other substances of abuse. Implementing the OAEOC routine elsewhere could result in better use of healthcare resources.

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137. Self-discharge during treatment for acute recreational drug toxicity: an analysis of four-years of Euro-DEN Plus presentations

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Objective: Self-discharge is a risk factor for readmission and mortality. We assess the rate of self-discharge from the emergency department (ED) among patients treated for acute recreational drug toxicity, and compare drugs taken, clinical features, and treatment between self-discharging and medically discharged patients.
Methods: The following data were extracted from the Euro-DEN Plus database on presentations to the ED with acute recreational drug toxicity to 32 centres in 22 European countries from 2014–2017: age, gender, drug(s) taken, clinical features, treatment, and disposition. Self-discharge was defined as taking one's own discharge or escaping from the ED before being medically cleared.
Results: Among the 23,947 presentations, 4,098 (17.1%) self-discharged, 13,973 (58.3%) were medically discharged from the ED, 1,434 (6.0%) were admitted to a critical care unit, 1,087 (4.5%) admitted to a psychiatric ward, 3,257 (13.6%) admitted to other hospital wards, 47 (0.2%) died, and in 51 cases (0.2%) disposition was not recorded. The proportion of self-discharge and medical discharge from the ED among cases involving amphetamine was 14.1% versus 60.1%, benzodiazepines 19.1% versus 57.1%, buprenorphine 30.3% versus 53.5%, cannabis 14.3% versus 65.2%, cathinones 20.7% versus 53.1%, crack cocaine 16.3% versus 55.6%, GHB 10.9% versus 53.8%, heroin 21.1% versus 57.6%, ketamine 16.4% versus 62.3%, LSD 11.4% versus 58.5%, MDMA 15.5% versus 61.9%, methadone 24.5% versus 49.6%, methamphetamine 11.3% versus 54.7, powder cocaine 14.6% versus 61.1%, pregabalin 39.8% versus 39.1%, synthetic cannabinoids 21.8% versus 46.1%, Z-drugs 32.7% versus 48.3%, other opioids 19.4% versus 53.4%, and unspecified/other new psychoactive substances (NPS)

Table 1. Comparison of self-discharging and medically discharged patients with acute recreational drug toxicity.

Parameter	Self-discharge (n = 4098) n (%)	Medical discharge (13,973) n (%)	p-value
Demographics			
Males[a]	3114 (76.0)	10 664 (76.3)	0.69
Age (years)[b,c]	32 (25–39)	31 (24–39)	<0.001
Clinical features			
Cardiac arrest[d]	11 (0.3)	9 (0.1)	0.002
Tachypnoea (>20/min)[d]	258 (6.3)	1081 (7.7)	0.002
Bradypnoea (<12/min)[d]	398 (9.7)	1015 (7.3)	<0.001
Vomiting	227 (5.5)	1369 (9.8)	<0.001
Hyperthermia (≥39 °C)	41 (1.0)	80 (0.6)	0.004
Headache	136 (3.3)	632 (4.5)	0.001
Anxiety	650 (15.9)	2657 (19.0)	<0.001
Hallucinations	229 (5.6)	749 (5.4)	0.60
Agitation	1100 (26.8)	2967 (21.2)	<0.001
Psychosis	185 (4.5)	613 (4.4)	0.76
Seizures	181 (4.4)	411 (2.9)	<0.001
Cerebellar features	109 (2.7)	396 (2.8)	0.59
Palpitations	274 (6.7)	1326 (9.5)	<0.001
Chest pain	237 (5.8)	994 (7.1)	0.003
Hypertension (≥180 mmHg)	212 (5.2)	558 (4.0)	0.001
Hypotension (≤90 mmHg)	150 (3.7)	454 (3.2)	0.22
Arrhythmias	29 (0.7)	98 (0.7)	1.00
Lowest level of consciousness[e]			0.83
Alert (GCS 15)	1353 (44.7)	4659 (44.8)	
Drowsy (GCS 9–14)	1242 (41.0)	4297 (41.3)	
Coma (GCS 3–8)	435 (14.4)	1448 (13.9)	
Treatment			
Treatment beyond observation	1693 (41.3)	6718 (48.1)	<0.001
Intubated	43 (1.0)	107 (0.8)	0.097
Sedation	542 (13.2)	2524 (18.1)	<0.001
Naloxone	620 (15.1)	1788 (12.8)	<0.001
Flumazenil	52 (1.3)	151 (1.1)	0.36
Other antidote	59 (1.4)	192 (1.4)	0.81

[a]Gender not registered in 2 cases. [b]Median (interquartile range). [c]Age not registered in 163 cases. [d]At presentation. [e]Glasgow Coma Score (GCS), lowest level of consciousness not registered in 4637 cases; self-discharge n = 3030; medical discharge n = 10404.

30.0% versus 45.7%. Table 1 shows comparisons of demographic data, clinical features, and treatment.
Conclusion: Self-discharge rates were higher for cases involving NPS and most depressant drugs, and lower for stimulants and GHB.

138. Just "nanging" around: case series of neurological sequelae from chronic nitrous oxide abuse

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Objective: "Nanging" refers to inhalation of nitrous oxide (N_2O) resulting in instant euphoria. N_2O use causes inactivation of vitamin B_{12} resulting in functional vitamin B_{12} deficiency, which can cause demyelination of the posterior and lateral columns of the spinal cord, and degeneration of large myelinated peripheral nerves. Recently, an emerging cluster of patients chronically abusing N_2O in Sydney, Australia has been noted. The objective was to evaluate cases of chronic N_2O abuse presenting with neurological symptoms to two toxicology units, to review the pathophysiology of subsequent neurological injury and to propose a treatment algorithm.
Methods: A retrospective review of patients presenting to two toxicology units in Sydney with reported chronic use of N_2O and neurological symptoms from July 2017 to July 2019. Medical records were reviewed for clinical details, treatment and outcomes.
Results: Eight patients were identified, 7 were female with a median age of 22 years (IQR: 19–26 years). All were students and 6 were of Asian background. Seven presented with decreased mobility and/or lower limb sensory deficits and one presented with psychiatric symptoms. They reported a median maximum use of 330 N_2O bulbs per day (IQR: 200-360, range: 50–720), for a median of 9 months (IQR: 4.5–24 months). All patients had an abnormal lower limb neurological examination including stocking sensory or proprioceptive loss and 7 had an abnormal gait at presentation. Seven had a low vitamin B_{12} and/or holotranscobalamin (active B_{12}) concentration except one who had prior intramuscular vitamin B_{12} supplementation. Three patients had evidence of bone marrow suppression with anemia and/or neutropenia. Magnetic resonance imaging (MRI) was performed in 7 of which 6 had changes consistent with subacute combined degeneration of the cervical and/or thoracic spinal cord. Three had nerve conduction studies; all were abnormal showing a demyelinating neuropathy. All 8 were treated with high dose intramuscular vitamin B_{12} and 4 with oral methionine. Of the 7 who presented with decreased mobility, all required prolonged physical rehabilitation. One improved, one was lost to follow-the remaining 5 had minor improvement and on longer-term follow-up had ongoing impaired mobility and sensory deficits.
Conclusion: Chronic N_2O abuse can result in serious long-term morbidity as a result of subacute combined degeneration of the spinal cord or peripheral neuropathy. This case series demonstrates that once neurological deficits are evident, they are not entirely reversible, despite treatment with vitamin B_{12}. Hence, it is important to educate high-risk student groups of the potential long-term sequelae of chronic N_2O abuse.

139. Drug-laced coffee packets: synthetic cathinones in Taiwan

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Objective: Synthetic cathinones have rapidly emerged as a concern in Taiwan in recent years. They are made into various products including bath salts, candies or instant beverage packets. Since early 2010, increasing numbers of drug-laced coffee or milk tea packets have been seized. These so-called "toxic coffee packets" or "toxic milk tea" usually contain synthetic cathinones, and may also be mixed with other illicit drugs, and because of the diversity of their ingredients, the clinical presentation of these cases can be complex and unpredictable.
Methods: We retrospectively review the patients who reported ingesting "toxic coffee packets" or "toxic milk tea" and presented to the emergency department (ED) of any Chang Gung Memorial Hospital branch in Northern Taiwan from 1 January 2015 to 31 August 2019.
Results: Overall 56 patients were included; 43 males (76.8%) and 13 females (23.2%), with mean age 29.4 ± 9.3 years. The most frequent presentation was palpitations (44.6%), followed by agitation (32.1%) and altered mental status (GCS <15, 30.4%) (Table 1). Tachycardia and hypertension were commonly seen. Fifteen patients (26.8%) had elevated creatine kinase or myoglobin and 10 patients (17.8%) developed acute kidney injury; one required transient hemodialysis. Hyponatremia was noted in 5 patients (10.4%). Most patients were discharged from the ED, 14 (25%) were admitted, of which 8 (14.3%) were admitted to an intensive care unit (ICU). A 37-year-old male patient developed agitation, seizure, ventricular tachycardia, and died. Confirmatory tests were available in 6 patients, and were positive for at least one synthetic cathinone.
Conclusion: Patients who reported ingesting "toxic coffee" or "milk tea packets" have a high chance of synthetic cathinone exposure. Cardiovascular and neurological symptoms were frequently seen after ingestion, and life-threatening cardiac arrhythmia can occur. Although most patients recovered after treatment and discharge from the ED, a small portion of patients need close monitoring and management in the ICU.

Table 1. Presentation, treatment and outcome 156 patients with toxic coffee/milk packet ingestion.

Parameter	N (%)	Parameter	N (%)
Presentations		**Treatments**	
Palpitation	25 (44.6%)	Gastric lavage	2 (3.6%)
Agitation	18 (32.1%)	Activated charcoal	2 (3.6%)
Altered mental status	17 (30.4%)	Benzodiazepines	28 (50.0%)
Hallucination	16 (28.6%)	Intubation	3 (5.4%)
Mydriasis	7 (12.5%)	Hemodialysis	1 (1.8%)
Tremor	7 (12.5%)	**Outcome**	
Nausea/vomiting	7 (12.5%)	Discharge from emergency department	30 (53.6%)
Sweating	6 (10.7%)	Left against medical advice	11 (19.6%)
Concomitant trauma	6 (10.7%)	Admission (ward + ICU)	14 (25.0%)
Delirium	5 (8.9%)	Intensive care unit admission	8 (14.3%)
Chest pain	5 (8.9%)	**Severity and outcome (Poison Severity Score)**	
Seizure	3 (5.4%)	No symptoms (PSS:0)	1 (1.8%)
Visual field defect	3 (5.4%)	Minor (PSS:1)	30 (53.6%)
Changes in vital signs		Moderate (PSS:2)	18 (32.1%)
Tachycardia	35 (62.5%)	Severe (PSS:3)	6 (10.7%)
Hypertension	22 (39.3%)	Mortality (PSS:4)	1 (1.8%)
Hyperthermia	4 (7.1%)		

140. Comparison of drugs involved in acute recreational drug toxicity presentations to the Emergency Department in young people versus adults reported to the Euro-DEN Plus project

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Objective: Existing public health data show differences in the prevalence of drug use in young people compared to older adults [1]. However, few data are available concerning the patterns of drug use reported in young people that present to the Emergency Department (ED) with acute recreational drug toxicity. This study examined the Euro-DEN Plus dataset to determine the drugs involved in acute drug toxicity presentations in young people compared to the larger adult patient group.
Methods: Data were examined from the Euro-DEN Plus dataset from January 2014 to December 2017. The "young" patient group was defined as those up to and including 18 years age, "adults" as those aged more than 18 years. Comparisons were made between groups for demographic characteristics, drug reported, clinical features and outcomes using chi-squared proportional tests.
Results: Age was not stated in 226 patients; the study population included 1384 young patients (5.8%) and 22337 adult patients (94.2%). A higher proportion of the young group were female (36.7% versus 23.1%). Young patients were more likely to report use of cannabis (42.2% versus 16.0%), ecstasy (15.5% versus 8.0%) and novel psychoactive substances (12.4% versus 8.4%) prior to presentation and less likely to report use of opioids (8.0% versus 33%), benzodiazepines (8.7% versus 18.0%), or cocaine (10.5% versus 21.8%). Symptoms differed between the groups: young patients were more likely to have palpitations (11.1% versus 8.1%), headache (7.2% versus 4.4%), and vomiting (19.3% versus 8.5%). Fewer young patients required mechanical ventilation (1.7% versus 3.3%) or critical care (3.5% versus 6.2%); a higher proportion were medically discharged from the Emergency Department (67.3% versus 58.0%); $p < 0.05$ for all comparisons. Overall mortality was similar in the young (0.1%) and adult groups (0.2%).
Conclusion: These data show differences in the type of drugs involved in acute recreational drug toxicity presentations to the Emergency Department in young patients, with consequent differences in symptoms and clinical outcomes. These results have implications for, and could inform the design of, harm reduction activities targeted at this specific age group.

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141. MDMA deaths in New South Wales, Australia

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Objective: 3,4-Methylenedioxymethamphetamine (MDMA), often referred to as ecstasy, is a commonly used recreational drug in Australia, that has recently been associated with a number of unintentional deaths. We aimed to identify the number of deaths in New South Wales (NSW) related to MDMA use over a 5-year period. We further aimed to classify these deaths by mechanism of death (poisoning, risky behaviour causing death or suicide), location and circumstances of use and toxicity from MDMA.
Methods: All deaths within the National Coronial Information System (NCIS) between 2013 and 2017 were searched for the term MDMA (and synonyms). Open cases were excluded (the majority of 2018/2019 cases remain open hence the years not included in this audit). Coronial reports, autopsy results, police reports and toxicology reports were then reviewed for each death.
Results: There were 2,644 coronial deaths in NSW where poisoning was ruled as the primary cause of death over the 5-year period. Sixty deaths (2.3%) included the term MDMA. Three cases were excluded as the coronial investigation was not completed, leaving 57 deaths. Of these, 18 (0.68%) were due to MDMA as the primary toxin, with the remaining 39 deaths unlikely to be due to MDMA effects. Of the 18 primarily MDMA-related deaths, 14 died due to the acute effects of MDMA poisoning, three died secondary to risky behaviour (one in a motor vehicle accident, two drowned) and one secondary to chronic effects of repeated use (delayed acute myocardial infarction). The median age of death was 26 years (range 19-54 years). Males were highly represented at 14:4 male:female deaths. Deaths by year were 2013:3, 2014:2, 2015:5, 2016:3 and 2017:5. Of the 14 acute poisoning deaths, seven occurred in the setting of MDMA use at a music festival. In all seven cases, MDMA was taken in the context of alcohol consumption, although in two cases alcohol was not measurable post-mortem. The dose of MDMA was often in excess of three tablets or unknown, and at least three users also consumed other substances. Four users collapsed during the festival, with the remaining three were found unresponsive the following morning. The setting of use of the remaining six acute poisoning deaths was nightclub (1), house-party (4) and home alone (1).
Conclusion: Whilst MDMA is recorded as a contributory factor in deaths within NSW, only a small number of deaths, < 1% of all poisoning deaths, are primarily caused by acute MDMA poisoning.

142. Transient delayed brain edema after consumption of synthetic cathinones

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Objective: Cathinone users are experienced drug users often co-consuming opioids [1,2]. As side effects, psychosis and behaviours leading to involuntary confinement are frequently encountered [3]. We report a patient with transient brain edema after cathinone use.
Case report: A 31-year-old male was admitted with delusions and agitation, reporting having used methylenedioxypyrovalerone (MDPV) and being substituted with methadone. Examination revealed conjunctivitis, mydriasis, hematomas on his legs, temperature 37.2 °C, respiratory rate 14/min, blood pressure 149/70 mmHg, heart rate 103/min, SpO_2 93% (room air), creatine kinase 1414 U/L (CK <174 U/L) and leukocyte count 13.91 g/L (4.0-9.0 g/L). He required sedation with benzodiazepines and was treated with antibiotics because of pneumonitis. Three days later, he was found in deep coma (Glasgow Coma Score [GCS] 3) and cyanotic. A cranial computerised tomography (CT) scan showed brain edema. Laboratory results did not show any abnormality. He received mannitol and dexamethasone and empiric therapy for encephalitis/meningitis. Magnetic resonance imaging (MRI) the next day and cranial CT scan demonstrated resolution of edema. Neurological examination showed deep coma, without neurological deficit and an electroencephalogram (EEG) showed no epileptiform discharges. Toxicological analysis by immunological assays and high performance liquid chromatography (HPLC) was positive for MDPV, benzodiazepines, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP), fluvoxamine, tetrahydrocannabinol (THC) and several opioids. After resolution of delirium he completely regained cognitive function.
Conclusion: Cerebral edema has been reported as a complication of synthetic cathinone use [4]; one case was diagnosed post-mortem after mephedrone use [5]. Breakdown of cerebral autoregulation or vasospasm may encourage the development of edema. Adulterants cannot completely be ruled out. Synthetic cathinones are a hazard to users and this case highlights a potentially lethal complication.

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143. Methadone poisonings admitted to the ICU: investigation of the predictive value of plasma methadone concentration and the required naloxone dose regimen

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Objective: Due to increasing prescriptions as maintenance therapy in opiate addicts in France, methadone is exponentially responsible for acute poisonings. Our objective was to investigate the circumstances of methadone overdoses; their clinical consequences and correlation between clinical severity and plasma methadone concentrations measured on admission; and the modalities of naloxone administration.
Methods: We conducted a retrospective single-centre observational study including all methadone-poisoned patients (proven by the measurement of plasma methadone concentration, measured using liquid chromatography coupled to mass spectrometry) admitted to the intensive care unit (ICU) in 2002-2018. Correlations were studied using Bartlett's sphericity tests and the Spearman coefficients were determined.
Results: Seventy-three methadone-poisoned patients (17 females/56 males, age of 37 years (33-44) [median (25^{th}-75^{th} percentiles)]) were included. Patients were chronic ethanol users (62%), active smokers (77%) and illicit drug users (79%). They were receiving long-term methadone treatment (30%) at a 60 mg (60-80) daily dose regimen. The circumstance of poisoning was related to the opioid dependence (80%), recreational use (10%), accident (9%) or suicide attempt (1%). The overdose combined benzodiazepines (72%), cocaine (57%) and ethanol (45%). The initial presentation included coma with Glasgow Coma Score of 11 (6-14), pinpoint miosis (84%) and bradypnea with respiratory rate of 14 breaths/min (10-18) responsible for alveolar depression [$PaCO_2$ of 49 mmHg (42-57)]. During the ICU stay, consciousness impairment worsened with Glasgow Coma Score of 3 (3-9). The patients required naloxone administration (71%) with initial intravenous bolus of 0.2 mg (0.2-0.4) allowing a sufficient reversal of the opioid toxidrome to avoid tracheal intubation which was finally required in 27% of the patients. The other complications included aspiration pneumonia (26%), QT prolongation (11%) and cardiovascular failure (4%). No fatality was reported. The plasma methadone concentration was 290 ng/mL (177-455) on admission, with no significant correlation with the Glasgow Coma Score, the respiratory rate and the $PaCO_2$.
Conclusion: Methadone overdose is responsible for life-threatening neurorespiratory depression that is reversible using low-dose naloxone. The absence of correlation between the plasma methadone concentration and the usual markers of neurorespiratory depression highlights the importance of the interindividual variability, mainly related to the coingestants and tolerance onset.

144. Clinical characteristics of analytically confirmed new psychoactive substance users in the emergency department: the experience of a tertiary medical center in Taiwan

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Objective: In the European Union, nearly 25% of the adult population has tried illicit recreational drugs in their lifetime. New psychoactive substances (NPS) are evolving rapidly in the recreational drug market. Since Asia is an influential source of NPS to the world, it is important to understand NPS trends in Asia. Emergency physicians play a crucial role in monitoring the health effects from NPS abuse. Our objective was to report the clinical characteristics of analytically confirmed cases of acute NPS intoxications presenting at the emergency department (ED).
Methods: We performed a retrospective study between May 2017 and August 2019 on patients presenting to our ED, a tertiary medical center in Taiwan, with positive urine illicit substance confirmed by liquid chromatography tandem-mass spectrometry (LC-MS/MS).
Results: Of 1,732 urine samples, 338 (19.5%) samples tested positive for more than one illicit substance by LC-MS/MS. There were various types of NPS in 115 patients (34.0%), including 75 (65.2%) with NPS abuse only and 40 patients (34.8%) had a combination of traditional substance and NPS abuse. Of 115 patients with at least one NPS detected in their urine, 98 cases were polysubstance abuse (85.2%). The most common NPS was ketamine (84, 73.3%) including three cases combined with other phencyclidine-type NPS, followed by synthetic cathinones (57, 49.6%) involving 19 types of synthetic cathinone. The most common synthetic cathinones were mephedrone (23/57, 40.3%), 4-methyl-α-ethylaminopentiophenone (4-MEAP, 14/57, 24.6%) and methylone (11/57, 19.3%). Although 4-MEAP occurred in 13 cases in 2017 and 2018, only one case was identified in 2019. Seven patients with ephylone use were found since 2019 and three cases had severe complications. Most patients were men (75.7%), and the average age was lower in the women (31.9 ± 10.1 versus 26.9 ± 8.7) ($P = 0.02$). The most common clinical presentation was agitation/violent behavior (35/115, 30.4%). Thirty-four cases (29.6%) were self-reported. Three cases were presented as out-of-hospital cardiac arrest and all were survived after aggressive resuscitation. Nineteen patients (19/115, 16.5%) were admitted to intensive care.
Conclusion: We present LC-MS/MS confirmed acute recreational drug intoxications at an ED in Taiwan. More than one-third of the cases were NPS abusers. Polysubstance abusers were common. Ketamine and cathinones were the most common NPS. The change of NPS trends especially the cathinone group was very rapid. Our cohort study could provide data on acute illicit substance toxicity and complications to improve recognition of the health impacts of NPS.

145. Mining and analysis of opioid content in longitudinal data posted in a social media forum

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Objective: Past studies have verified that publicly available social media data may be mined to discover information regarding prescription and illicit opioid use [1]. Our objective was to qualitatively study whether anonymous data from Reddit may be utilized to describe longitudinal information posted by people who self-reported opioid use.
Methods: We first identified three sample subreddits (/r/drugs,/r/opiates and/r/suboxone) that contain self-reported accounts of drug use. We then employed natural language processing to identify users who had mentioned opioid keywords (prescription or illicit) in their posts. We randomly selected 5 users from this subset, and collected all their available past posts from Reddit for manual analysis of the relevant longitudinal information posted by them. In particular, we tried to find information regarding illegal drug use (types and quantities of drugs consumed), demographics (age, race/ethnicity, gender, location), and clinical and social impacts (if any) of drug usage.
Results: From 5 anonymous users, we were able to collect a total of 4,288 posts spanning from September 2016 to January 2019. All 5 users made their gender information available (4 males, 1 female), 3 mentioned their ages, and 4 mentioned locations. The longitudinal timelines of the users revealed a variety of other information including, but not limited to:

i. their use of illicit (e.g., heroin, cocaine, 3,4-methylenedioxymethamphetamine [MDMA], kratom) and nonmedical use of prescription drugs; all five reported opioid addiction;
ii. social impacts of their drug use – loss of employment, inability to continue education, financial stress caused by expenses associated with addiction, loss of social life, family and friends, social isolation, loss of parental trust, imprisonment;
iii. clinical consequences of addiction – ranging from adverse reactions such as headache, sweating, insomnia, vomiting to withdrawal, drug overdose and suicidality;
iv. challenges of opioid addiction and reoccurrence of use.

Conclusion: Our study shows that longitudinal data analysis of anonymized social media participants who self-report opioid use may provide important information which is not available from individual posts or other data sources. With the current state of the opioid crisis, further research in this domain is warranted, particularly in how this knowledge can be utilized.

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146. 2,4-Dinitrophenol (DNP) interest, exposures and deaths in Australia following restrictive re-scheduling

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Objective: 2,4-Dinitrophenol (DNP) is a weight loss agent that gained popularity in the 1930s but was banned due to safety concerns. There are several recent reports of a resurgence in DNP use internationally. Due to concerns over toxicity and increasing use, DNP was up-scheduled in Australia in February 2017 to Schedule 10, defined as "substances of such danger to health as to warrant prohibition of sale, supply and use." We aimed to examine DNP poisonings, deaths, and Internet search interest in Australia, including the effect of the 2017 legislation.
Methods: A retrospective study of DNP exposures reported to the New South Wales Poisons Information Centre (NSWPIC, Australia's largest PIC, taking 50% of the nation's poisoning calls), deaths in the National Coronial Information System (NCIS, Australia's database of coronial records), and Google Trends search interest, 2004–2018.
Results: There were 24 DNP exposures in the NSWPIC database, with an increase in cases in recent years (15/24 occurred since January 2017). The majority of patients (71%, n = 17) were male. The majority 83% (n = 20) were adults aged 20-74 years, and 67% (n = 16) of cases were intentional exposures (includes intentional misuse, recreational use, deliberate self-poisoning). Most patients (92%, n = 22) were in hospital at the time of call or referred to hospital by the PIC. A range of symptoms were reported at the time of call, with the most common being tachycardia (7 cases), hyperthermia (4), shortness of breath (4), weakness (4) and chest pain (3). There was one death in the NSWPIC database, an adult male who had taken four DNP capsules, who rapidly developed tachycardia, hypertension, tachypnoea, and reduced level of consciousness, progressing to cardiac arrest within 2 hours of ingestion. The substance was analytically confirmed to be DNP. There were three more deaths (two male, one female, age range 19-34 years) attributed to DNP in the national coronial database. All four deaths occurred since 2015, with two since the 2017 rescheduling. Google trends showed increasing search interest in Australia, including a doubling of search interest from 2010 to 2015.
Conclusion: Although DNP exposures are uncommon, there has been a rapid increase in cases in Australia, including four recent deaths. This is despite restrictive rescheduling in 2017. This is the first Australian study examining time trends in DNP exposures and search interest, highlighting the need for action to prevent further harms. Targeted action by police forces, local education in gyms, and increased screening of the incoming mail supply are potential strategies.

147. Severe acidosis and prolonged coma after a massive overdose of gamma-hydroxybutyrate (GHB)

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Objective: Gamma-hydroxybutyrate (GHB) is used, in doses of a few millilitres, for recreational purposes. However, the therapeutic range is narrow and intoxications presenting with central nervous depression are common. In addition, bradycardia, hypotension, hypoventilation and mild hypothermia may also occur. Symptoms are typically short-lived, resolving after a few hours and the plasma elimination half-life is reported to be 30-50 minutes [1]. Severe metabolic acidosis, probably caused by GHB itself, has previously been described in one case with an extreme overdose [2]. Presented here is a case of massive GHB intoxication with severe acidosis and prolonged symptoms.
Case report: A 32-year-old male arrived at the hospital after ingestion of 500 mL of GHB-solution as a suicide attempt. On arrival he was deeply unconscious (Glasgow Coma Score [GCS] 3). His blood pressure was 80/40 mmHg, and his heart rate 58 bpm. In addition, he had a combined respiratory and metabolic acidosis: pH 6.95, $PaCO_2$ 9.5 mmHg, base deficit −16.3 mEq/L, lactate 1.7 mmol/L, anion gap 30 mmol/L and calculated osmolal gap 5 mmol/L. The blood concentration of GHB obtained approximately 120-150 minutes postingestion was 940 mg/L. He was promptly intubated. The hypotension resolved with administration of intravenous Ringer's acetate and a low dose of norepinephrine. His acidemia normalised without additional treatment during the subsequent (12) hours. However, the central nervous depression had a prolonged cause, disabling extubation until 75 hours after admission to the hospital. After extubation he was disoriented and distressed. Another three days later he was discharged to a psychiatric clinic.
Conclusion: This case supports earlier findings that massive GHB intoxication may lead to profound acidosis. The blood concentration of 940 mg/L indicates a severe intoxication. The prolonged unconsciousness does not correspond to the reported elimination half-life of 30-50 minutes, however, it has been postulated that, in high doses, GHB is eliminated according to zero-order kinetics (proposed elimination rate 18 mg/L/hour) rather that first order kinetics, thereby prolonging elimination [1]. Presuming that the acidosis is caused by GHB accumulation, the assumption of zero-order kinetics and prolonged elimination could also explain the prolonged acidosis.

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149. Gamma-hydroxybutyrate (GHB) in nightlife settings and effectiveness of an on-site harm-reduction organization

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Objective: Gamma-hydroxybutyrate/gamma-butyrolactone (GHB/GBL) is abused at music events and parties. The main symptom of GHB/GBL overdose is a sudden and short-lasting unconsciousness. Symptoms typically resolve within a few hours allowing management on site. The non-profit harm reduction organization DrogArt is providing crisis intervention and support to distressed, injured and/or unconscious partygoers in their Silent Rooms (SR) and separate on-site facilities for interventions. Although they cooperate closely with paramedics, recognizing life-threatening GHB/GBL overdose still presents a challenge. The aim of this study was to evaluate interventions of DrogArt in GHB/GBL-overdosed partygoers.

Methods: In this retrospective study we collected data from 2014 to 2018 on all GHB/GBL-overdosed partygoers handled by DrogArt in Ljubljana, GHB/GBL overdosed patients admitted to the Emergency department (ED) of the University Medical Centre Ljubljana, and autopsy reports positive for GHB at the Institute of Forensic Medicine Ljubljana. We defined GHB/GBL overdose as self-reported GHB/GBL use and/or GHB/GBL confirmation by liquid chromatography/mass spectrometry (LC-MS). Suicide attempts were excluded. We gathered data on clinical presentation, toxicological results and outcome. A comparison was made using the 2-sample proportion test and t-test for independent values.

Results: In the 5 year study period, 985 interventions were provided by DrogArt, of which 72 were in GHB/GBL-overdosed partygoers. Twenty-one GHB/GBL-overdosed party attenders assessed on site in the SR were unconscious, 14 agitated and 15 vomited. Paramedics removed 9 of 72 GHB/GBL-overdosed partygoers due to coma and/or shallow and slow breathing, one of them was intubated and ventilated at the emergency department (ED). The remaining 63 partygoers were sent home after their symptoms improved. Additionally 123 GHB/GBL-overdosed partygoers were admitted to the ED from different parties not covered by DrogArt. Sixteen of those were intubated and ventilated at the ED. The patients requiring intubation and ventilation differed from other GHB/GBL-overdosed patients in concomitant cocaine abuse ($p = 0.008$), but not regarding age, gender, ethanol or other drug use and symptoms on site, including unconsciousness ($p = 0.08$). Seven conscious patients needed intubation during subsequent treatment at the ED. GHB/GBL overdose was confirmed by LC-MS in 28% of admitted patients. DrogArt reduced ED use for GHB/GBL overdose patients by 37%. No one died due to GHB/GBL overdose in Ljubljana over the study period.

Conclusion: Non-profit harm reduction organization volunteers efficiently recognize GHB/GBL-overdosed partygoers who do not need admission to the ED. Their interventions reduce the burden of GHB/GBL overdose. Concomitant abuse of cocaine in these patients increases the risk for intubation.

150. Treatment with naloxone and follow up after opioid overdose outside of hospital: observational data 2014-2018 in Oslo, Norway

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Objective: Guidelines for prehospital naloxone use in Oslo, Norway, have shifted from intravenous (IV) use to intramuscular (IM) administration in the last decade, with focus on titration to effect. The aim has been to reduce opioid withdrawal and thus increase cooperation and transport to further care and follow-up. This study investigates this change in treatment and what type of care and follow-up the patients receive.

Methods: Patients treated with naloxone in Oslo City Centre between 2014 and 2018 were included. Patients received information about registration and could withdraw. Data were collected from medical records and were analysed in STATA 15.1. The study was approved by the Regional Ethics Committee.

Results: Overall 2215 cases of naloxone administration were recorded; 901 unique patients had 1751 events while 464 cases were registered anonymously. Most (75%) were men, mean age was 38 years. The first naloxone treatment was IM in 92%, IV in 2%, IM + IV in 4% and by other routes in 3%. A second dose was given in 15%, and 3% needed three or more doses of naloxone. The initial IM naloxone dose was 0.4 mg in 39% and 0.8 mg in 59% of the patients. Most patients (57%) were left at the scene; of these, 57% were left at a safe injection facility or institution and 43% at home or a public place, all against medical advice. In total 28% were followed up by primary care, 13% were taken to hospital and 1% received other follow up. Time in care for those left on scene was on average 33 minutes (SD 13).

Conclusion: Naloxone doses are smaller than previously used, with less use of intravenous naloxone [1]. The proportion of the patients left on site after naloxone treatment reduced from 76% in 2003-4 to 57% in the current study [2]. One of the reasons for this change may be more gentle use of naloxone, which should be considered in guidelines to reduce the number of patients left against medical advice.

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151. Accelerated idioventricular rhythm with recreational 1,4-butanediol overdose

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Objective: To report a case of 1,4-butanediol (BD) overdose manifesting with an accelerated idioventricular rhythm not associated with myocardial ischaemia/infarction.
Case report: A 45-year-old male was found by paramedics with Glasgow Coma Score (GCS) 7 (E1V1M5), a regular pulse rate of 40/minute, normotensive, respiratory rate 12/minute, saturating 96% (room air) and afebrile. The patient retrospectively reported ingesting 6 mL "GHB" approximately 25 minutes prior to paramedic arrival, with nil other coingestants. An electrocardiogram (ECG) 35 minutes post-ingestion showed sinus bradycardia (pulse 52/minute) with normal axis and median QRS and QT durations of 110 and 440 ms, respectively. At 1 hour post ingestion, repeat ECG showed absence of P waves, regular QRS rate 61/minute, with median QRS duration 200 ms with left bundle branch block morphology and discordant T waves. A repeat ECG 10 minutes later revealed sinus rhythm. Blood tests including serum biochemistry, glucose, liver function tests and venous blood gas analysis were normal. The patient was managed conservatively. Continuous cardiac monitoring did not demonstrate other dysrhythmias. The patient did not report cardiac symptoms at any time. At 6 hours post-ingestion the patient was clinically at baseline, and discharged at 12 hours post-ingestion. Serial high sensitivity troponin I were 4 and 3 ng/L at 1.5 and 11 hours post ingestion, respectively (reference range <20 ng/L). A transthoracic echocardiogram 18 hours post-ingestion demonstrated normal ventricular structure and function. Comprehensive drug testing on whole blood by liquid chromatography-mass spectrometry was positive for 1,4-BD (7 mg/L, 0.08 mM) and gamma-hydroxybutyrate (GHB) (110 mg/L, 1.06 mM) at 1.5 hours post-ingestion; no cardiotoxic drugs were present.
Conclusion: Various ECG abnormalities associated with GHB intoxication are reported including 1st degree heart block, right bundle branch block and the appearance of U waves [1], however all these patients were exposed to pro-arrhythmic coingestants. In a paediatric GHB exposure, transient right bundle branch block pattern and ST elevation were observed [2], suggesting that GHB can impair cardiac conduction in isolation. There is no literature indicating that 1,4-BD has pro-dysrhythmic effects in isolation. This report demonstrates that 1,4-BD and/or GHB exposure can induce a transient accelerated idioventricular rhythm.

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152. Acute intoxication with α-pyrrolidinohexiophenone, 4-fluoromethylphenidate and aminopropylbenzofuran complicated with rhabdomyolysis: a case report

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Objective: New psychoactive substances (NPS) can induce potentially dangerous clinical effects. We present a case of acute intoxication by synthetic cathinones that caused intense psychomotor agitation and rhabdomyolysis requiring intensive care management.
Case report: A 34-year-old Caucasian male, affected by substance use disorder and obsessive-compulsive disorder, was admitted to the emergency department complaining of psychomotor agitation after exposure to synthetic cathinones. Clinical observation in a non-intensive care unit was offered, but he refused and left the hospital against medical advice. After 17 hours, he was found confused and agitated and was transported back to the hospital, where he was admitted in a non-critical care unit. Sedation with continuous diazepam (IV) and olanzapine (IM) was started, as well as crystalloid fluids due to high concentrations of creatine phosphokinase (CPK) (28,474 IU/L) and myoglobin (159 ng/L). His clinical condition and blood tests improved on day 4 of hospitalisation (CPK 1,266 IU/L, myoglobin 94 ng/L), and he was discharged fully recovered on day 5. Urine samples obtained on admission were analysed by gas chromatography-mass spectrometry (GC-MS), liquid chromatography-mass spectrometry (LC-MS) and liquid chromatography-tandem mass spectrometry (LC-MS/MS) were positive for 4-fluoromethylphenidate (4F-MF), α-pyrrolidinohexiophenone (α-PHP), aminopropylbenzofuran (APB) and amphetamines.
Conclusion: NPS can produce serious effects on the central nervous system and other organs, however, few data are present in the literature describing clinical cases and their management. To this regard, only few clinical cases of α-PHP intoxication have been published, including one of fetal death at week 36 in a pregnant woman who consumed α-PHP throughout pregnancy [1]. There are few cases of intoxication and fatality reported following the use of both 4F-MF [2] and APB [3]. The clinical case we present gives an example of how timely sedation and intravenous hydration could potentially reduce toxicity and prevent the progression to kidney failure in such cases.

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153. Severe amyl nitrite poisoning in a sex shop

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Objective: Amyl nitrite is used as an antidote in cyanide poisoning and recreationally for its aphrodisiac properties and for its vasodilation effect. It causes oxidation of iron in haemoglobin from ferrous (Fe^{2+}) to ferric (Fe^{3+}) to form methemoglobin. Nitrites may be absorbed and cause poisoning via ingestion, inhalation, injection or skin absorption. Medical observation is recommended for all ingestions as 0.7 to 6 g may be lethal. Levels of methemoglobinemia above 50% may be lethal. An unusual case of intoxication which required antidote treatment is presented.
Case report: A 39-year-old male patient was found unconscious, cyanotic, with hoarseness and foam around the mouth on the floor of the sex shop at about 7 pm. According to the shopkeeper, he had arrived inebriated and mentioned he had drunk 1 L of wine and 2 beers and used some illegal drugs. On arrival of the emergency service his Glasgow Coma Score was 3, pupils were isocoric, and no trauma was present. His blood pressure was 135/85 mmHg, pulse 80/min, respiratory rate 14/min, and pulse-oximetry (SpO_2) 94%. He was intubated and ventilated. On admission to the Intensive Care department the whole body of the patient was cyanotic grey, and he had mild tremor and trismus. No cardiovascular or respiratory clinical impairments were found; his electrocardiogram (ECG), echocardiography, computerised tomography (CT) and angiography of the brain were normal. Cyanosis was profound even after oxygen supply and ventilation. Toxicological analysis revealed methemoglobinaemia of 62.5%. The Toxicologic Information Centre (TIC) was contacted and toluidine blue was provided from the stock of the TIC. The first dose of toluidine blue (40 mg/kg) was administered intravenously around midnight, and 3 minutes later the patient began to wake up. After the second dose of antidote the SpO_2 increased from 86% to 100%. Sedation was used as the patient was restless. When he was extubated in the morning, his vital functions were normal, and his urine was green/bluish due to the antidote use. He admitted to ingestion of amyl nitrite and now understands its danger in high doses; he did not specify the amount taken. He was discharged in a good condition.
Conclusion: Amyl nitrite is used as a party drug and aphrodisiac, frequently with no understanding of the dangers and risks it involves. Unless the antidote (toluidine or methylene blue) is promptly administered, the exposure may be life-threatening. It is well known that SpO_2 may be misleading as it does not reflect oxygen desaturation even at high methemoglobin concentrations.

Acknowledgement

Progres Q25/1LF and Q29/1LF.

154. Bilateral globus pallidus necrosis and delayed neurologic sequelae following acute n-ethylpentylone poisoning

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Objective: Synthetic cathinones are widely used for recreational purposes. Acute poisoning by cathinones can manifest various effects such as agitation, seizures, delirium, serotonin syndrome, and coma. However, the development of bilateral globus pallidus necrosis and delayed neurological sequelae (DNS) similar to those caused by carbon monoxide poisoning had not been reported. We herein report a patient manifesting bilateral globus pallidus necrosis and DNS after n-ethylpentylone poisoning.
Case report: A 39-year-old man was found unconscious in his home. When he arrived at the emergency department of a local hospital, he manifested high fever (40.7 °C), tachycardia (137/min), confusion, profuse sweating, urinary incontinence, and mydriasis. Laboratory data were remarkable for leukocytosis, acute kidney injury (serum creatinine 2.65 mg/dL) and rhabdomyolysis (creatine kinase 18,451 U/L). Brain computerised tomography (CT) scan disclosed hypodensity of the bilateral globus pallidus. He was then transferred to a medical center and admitted to the intensive care unit. After admission, he gradually regained consciousness. Moreover, his rhabdomyolysis and acute kidney injury improved rapidly after receiving adequate hydration. Urine toxicologic screening disclosed the presence of benzodiazepines, ketamine and n-ethylpentylone. Despite the above-mentioned improvements, the patient had persistent fever and both chest radiograph and CT scan showed diffuse consolidations and nodules in bilateral lung fields. Hypersensitivity pneumonitis was diagnosed by bronchoalveolar lavage. Steroid treatment was commenced and his fever subsided. Pulmonary tuberculosis was diagnosed 5 weeks later by bronchoalveolar lavage fluid culture and was treated accordingly. In addition to pulmonary lesions, the patient was found to have memory impairment, progressive limb weakness, ataxia and psychomotor retardation after 3 weeks of admission. Brain magnetic resonance imaging (MRI) showed mixed restricted diffusion, high signal change and susceptibility effect in bilateral globus pallidus on T1-weighted image, suggestive of hemorrhagic necrosis. Diffuse cerebral leukoencephalopathy was also noted. Delayed neurologic sequelae was diagnosed and the patient received long-term rehabilitation. The patient exhibited progressive improvement of cognitive function and muscle power, and could walk without assistance 6 months later. A follow-up brain MRI at 7 months post-exposure showed bilateral globus pallidus cavitation and calcifications with resolution of leukoencephalopathy. One year after the poisoning, the patient manifested only mild clumsiness of his left hand.
Conclusion: We report a patient who manifested bilateral globus pallidus necrosis and DNS following n-ethylpentylone poisoning. Although the exact mechanisms remain unclear, we propose that an ischemic insult, vasculitis and toxicity of excessive neurotransmitters may be responsible for the unique effects observed in this patient.

155. The development of poisonings with illegal substances: data from the Danish Poisons Information Centre (DPIC)

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Table 1. The development of poisonings with illegal substances 2007-2018. *Nitrous oxide is not an illegal substance in Denmark.

Year	Cocaine	Cannabis	MDMA	Amphetamine	GHB	Ketamine	Heroin	LSD	Nitrous oxide*	All calls to DPIC
2007	104	75	80	114	49	24	28	22	0	11,860
2008	125	105	80	144	70	31	42	17	0	13,241
2009	101	89	59	134	73	32	25	18	0	17,434
2010	136	113	58	202	105	48	31	10	0	18,127
2011	150	125	86	239	128	44	28	20	1	19,584
2012	127	126	104	169	109	40	28	7	4	20,851
2013	154	148	112	191	96	54	29	26	2	23,242
2014	203	154	159	168	124	48	42	45	2	24,782
2015	225	179	145	164	113	37	37	34	16	25,406
2016	244	132	168	173	72	45	43	33	22	27,500
2017	289	202	160	163	89	41	28	33	18	29,158
2018	298	189	182	154	141	67	49	30	39	31,530

Objective: Since the DPIC started in 2006, inquiries regarding illegal substances have been recorded. In general, they account for less than 10% of all calls but represent cases with severe and sometimes fatal outcome. By comparing data from the DPIC and drug seizure data from the Danish Health Authorities, we aimed to evaluate the trends of illegal substance use.
Methods: A retrospective study of DPIC records from 2007-2018 regarding illegal substances involving a patient with symptoms of intoxication. Cases with a positive urine screening test bedside and no clinical history of drug exposure were excluded.
Results: An increase in total calls was observed in the study period (Table 1). The majority of calls involved cocaine, amphetamine, cannabis, 3,4-methylenedioxymethamphetamine (MDMA) and gamma-hydroxybutyrate (GHB). The remaining were substances with less than 100 inquiries per year. Until 2013 amphetamine was the drug with the most inquiries, but since 2014 cocaine has been the most frequent drug. New trends include GHB, especially since 2010, and nitrous oxide since 2015.
Conclusion: The increase in inquiries concerning illegal substances was partly due to an increase in all calls to the DPIC. The weakness of the study is that validated confirmatory tests on blood or urine are unavailable in Denmark. Cocaine as the most prevalent illegal substance reported to the DPIC correlates with drug seizure data from the Danish Health Authorities, also reporting an increase since 2010 [1]. In the report cannabis seizure is seen more than three times as often as cocaine in 2017, but this trend is not seen in the DPIC data, most likely because the use of cannabis rarely leads to hospital contact.

Reference

[1] The Danish Health Authorities. [Drug crime, drug seizures and the drug market]. 2018 [cited 19 Oct 2019]. Available from: https://www.sst.dk/da/udgivelser/2018/~/media/A49333D5459C4321883F8F2CF889CE2E.ashx. Danish.

156. Global interest in tramadol and polysubstance use

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Objective: The objective of this study was to conduct an epidemiological study of tramadol non-medical use (NMU), misuse, abuse, and diversion from five countries in Europe (EU5) in order to test the hypothesis that tramadol NMU was similar to opioid comparators across different countries and study populations. These analyses provide country-specific, polysubstance analyses of tramadol NMU when compared to opioid comparators in different study populations. Populations included the general public, entrants to treatment, and exposure cases reported to poison centres.
Methods: Data from the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System programs, including exposures reported to poison centres, and general population and treatment centre patient surveys, were analyzed as available during various periods between 3rd quarter 2010 to 4th quarter 2018. Tramadol NMU, relative ranking of outcomes, and prevalence of outcomes were compared to comparators morphine, oxycodone, and codeine. Polysubstance analyses in diverse populations were also conducted across countries wherever data were available.
Results: The RADARS System study found that tramadol NMU was as common as comparators accounting for availability and the prevalence of outcomes was lower relative to less available. Across four EU countries, polysubstance analyses in the general population found that among those who have non-medically used tramadol, approximately half non-medically used only tramadol and no other opioid; similar proportions were observed among those who misused and abused. Among entrants to treatment with opioid use disorder, polysubstance use was common; less than a third of respondents reported only tramadol abuse.
Conclusion: This study found that, in general, tramadol NMU did not differ drastically relative to that of comparators when studying prevalence of outcomes and polysubstance use in diverse study populations and in different countries. Poison centre exposure calls, abuse proportions of treatment centres entrants, and general population misuse population rate data support the hypothesis.

Table 1. Rates of tramadol non-medical use, misuse, and abuse: RADARS® System Programs.

Type of Data	Tramadol Outcome	France	Germany	Italy	Spain	UK
NMU, Misuse, and Abuse of Tramadol						
Poison centre calls (GTNet)	NMU Rate Rank	1. Codeine 2. Tramadol 3. Morphine 4. Oxycodone	1. Morphine 2. Tramadol 3. Oxycodone 4. Codeine			1. Codeine 2. Tramadol 3. Morphine 4. Oxycodone
Paper survey of entrants to treatment centre programs (Europad)	Abuse Proportions (95% CI)[a]	0.03 (0.02, 0.05)	0.07 (0.04, 0.10)	0.10 (0.06, 0.16)	0.06 (0.04, 0.11)	0.10 (0.09, 0.12)
Calibrated general population online survey (NMURx)	NMU Population Rate (95% CI)[b]		1,222 (1,053, 1,392)	348 (248, 448)	2,931 (2,489, 3,373)	1,688 (1,459, 1,917)
	Misuse Population Rate (95% CI)[b]		1,180 (1,013, 1,347)	344 (244, 444)	2,900 (2,458, 3,341)	1,621 (1,395, 1,847)
	Abuse Population Rate (95% CI)[b]		129 (75, 183)	79 (35, 124)	223 (139, 307)	335 (247, 424)
	Diversion Population Rate (95% CI)[b]		359 (264, 454)	200 (127, 273)	1,318 (1,106, 1,530)	1,158 (969, 1,348)

[a]Proportions for entrants to treatment are out of all entrants providing valid surveys
[b]Rates for the general population survey are national rates per 100,000 adult population
Grey cells indicate data not obtained or unavailable for the country/outcome combination.
NMU: Non-medical use; CI: 95% Confidence interval.

157. Characteristics of ecstasy toxicity in a Norwegian cohort of hospitalized poisoned patients

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Objective: Ecstasy (MDMA) is an amphetamine derivative with more hallucinogenic properties compared to amphetamine. The proportion of people in Norway reporting ecstasy use has increased in recent years [1]. We wanted to examine differences in clinical features between overdosed patients with positive versus negative analysis for ecstasy.
Methods: Case series of patients presented at Oslo University Hospital after acute poisoning with recreational drugs were collected from October 2014 to December 2018. Patients with drug analyses performed on both immunoassay and mass spectrometry samples were included. Drug analyses were performed on 367 of 819 patients, of which 73 (20%) returned positive on ecstasy. Differences in proportions were calculated using Pearson chi-squared test, differences in continuous variables were calculated using Student t-test.
Results: Patients in the ecstasy group were younger than the non-ecstasy group (30.3 versus 34.5 years, $p = 0.001$) and with a tendency towards more females (34% versus 26%, $p = 0.15$). More patients in the ecstasy group hallucinated (41% versus 21%, $p < 0.001$), and were hypertensive (33% versus 16%, $p < 0.001$). Correspondingly, there was a tendency of less patients hypotensive in the ecstasy group (18% versus 28%, $p = 0.054$). There were no significant differences in anxiety, agitation, psychosis, intubation rate, hyperthermia or GCS (Table 1). In the ecstasy group, 71 of 73 (97.3%) combined ecstasy with other recreational drugs (76.8% with more than one): amphetamine 89%; benzodiazepine 70%; cannabinoid 52%; other opiates (including heroin) 38%; cocaine 27%; buprenorphine 12%; gamma-hydroxybutyrate (GHB) 7%; methadone 5%.
Conclusion: In patients hospitalized with acute recreational drug toxicity, blood drug analysis revealed ecstasy use in 20%. Ecstasy-positive patients were younger, hallucinated more frequently and were more hypertensive than other patients.

Table 1. Clinical data for 3,4-methylenedioxymethamphetamine (MDMA, ecstasy) patients presented at Oslo University Hospital.

	Analysis with positive ecstasy		Analysis with negative ecstasy		
Parameter	n = 73, n (%)	95% CI	n = 294, n (%)	95% CI	p-value
Length of stay (hours)	29.44 (mean)	(18.2-40.7)	34.72 (mean)	(28.8-40.6)	0.559
Gender	25 (34) female		76 (26) female		0.151
Age[##]	30.3 (mean)	(28.4-32.2)	34.54 (mean)	(33.4-35.67)	<0.001*
Anxiety	56 (77)		218 (74)		0.653
Hallucination	30 (41)		63 (21)		<0.001 *
Agitation	41 (56)		140 (48)		0.192
Psychosis	9 (12)		35 (12)		0.921
Hypertension	24 (33)		47 (16)		<0.001*
Hypotension	13 (18)		85 (28)		0.054
Intubated	19 (26)		75 (25)		0.586
Glasgow Coma Score (GCS)[##]	8.15 (mean)		8.27 (mean)		0.804
Hyperthermia	8 (11)		65 (22)		0.884

[#]Pearson Chi-Square test; [##]Independent T-test; *Significant p-value <0.001.

Reference

[1] Norwegian Institute of Public Health. Substance use disorders in Norway, 2019 [cited 19 Oct 2019]. Available from: https://www.fhi.no/en/op/hin/mental-health/substance-use-disorders-in-norway/

158. Change of quality of life in prescription opioid patients after rapid opioid detoxification

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Objective: To confirm or refute the hypothesis that rapid opioid detoxification improves quality of life for chronic pain patients with long-term prescription opioid usage.
Methods: Our retrospective study included 35 patients who underwent rapid opioid detoxification in the years 2010-2019. Patient pain levels and quality of life were evaluated three times using the SF-36v2 form before, after the treatment and a minimum 3 months later. Data was analyzed using MS Excel and IBM SPSS 23.0 software, statistical significance was assumed when $p < 0.05$.
Results: Follow-up was completed by 15 patients (males 60% ($n = 9$), average age 64.7 ± 14.1 years), Overall 53.3% ($n = 8$) were in full remission, and the remaining 7 patients (46.7%) used either the same medications in the same doses (42.9%), less of different prescription opioids (28.6%), or the same medication in reduced doses (28.6%). Seven patients (42.9%, males 50%) had a relapse in 6-18 months (42.9%) or right after the detoxification (57.1%). A decreased pain level after detoxification was indicated by 12 patients (80%) and 86.6% ($n = 13$) of patients indicated better quality of life compared to that before the treatment ($p = 0.00023$).
Conclusion: Significant pain reduction and quality of life improvement was observed in the majority of patients and full remission was reached by some patients after rapid opioid detoxification treatment. This has been attempted in one other study, but without patient quality of life evaluation [1]. Our results lead us to believe that this treatment can be safely administered. Further life quality follow-up studies would be beneficial in order to evaluate the effects of rapid opioid detoxification.

Reference

[1] Monterubbianesi MC, Capuccini J, Ferioli I, et al. High opioid dosage rapid detoxification of cancer patient in palliative care with the Raffaeli model. J Opioid Manag. 2012;8:292–298.

159. Analytically-confirmed exposure to *N*-ethylpentylone in the UK: a report from the IONA study

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Objective: The Identification Of Novel psychoActive substances (IONA) study has been analysing clinical samples from those attending emergency departments across the UK with suspected severe toxicity caused by new psychoactive substances (NPS). In view of the limited information available currently about human toxicity [1], clinical features of 3 patients are described where the ring-substituted synthetic cathinone *N*-ethylpentylone (NEP, also called *N*-ethylnorpentylone) was detected in patient samples.
Methods: Patients (≥16 years) presenting to participating hospitals with severe acute toxicity (pre-defined definitions) after suspected NPS exposure were included after informed consent (or agreement of a relative/representative for those lacking capacity). Demographic and clinical features were recorded using a structured data collection sheet. Blood and/or urine samples were analysed by liquid chromatography-tandem mass spectrometry.
Results: Of 471 patients with analytical and clinical data available, NEP was detected in samples from 3, all males. None reported use of NEP, but two had used other stimulants and the other had taken an unknown tablet. Sample analysis revealed other drugs of misuse in samples from all 3 patients. Clinical features, consistent with those of other cathinones, included agitation, hallucinations or psychosis (3), tachycardia (2), hypertension, mydriasis, clonus and raised creatine kinase (1 each). Two patients had reduced level of consciousness; co-used sedative drugs (chlordiazepoxide, 5F-NPB 22) were detected in samples from both. No serious complications were reported and all 3 discharged themselves from hospital 6 to 133 hours after admission (Table 1).
Conclusion: NEP was detected infrequently in this large UK patient cohort. Those affected did not report its use, suggesting possible inclusion of NEP in tablets/preparations sold as other substances, as previously reported [1]. Recorded clinical features are consistent with those of other cathinones, but co-used substances will also have contributed.

Reference

[1] World Health Organization. Critical review report: N-ethylnorpentylone [cited 4 Oct 2019]. Available from: https://www.who.int/medicines/access/controlled-substances/N-Ethylnorpentylone.pdf

Table 1. Clinical details of 3 male patients with exposure to N-ethylpentylone (NEP).

	Male 1	Male 2	Male 3
Presentation date	August 2016	April 2017	August 2018
Location	South East England	South East England	Scotland
Reported exposure(s)	Unknown tablet	Mephedrone	Amphetamine, MDMA
Route	Oral	Snorted	Oral
Positive analytical findings	NEP, Chlordiazepoxide	NEP, Butylone, 5F-NPB 22	NEP, Amphetamine, Methamphetamine, MDMA, Diazepam
Clinical features	Agitation, Hallucinations, Tachycardia (126/min), Hypertension (systolic BP 183 mmHg), Increased creatine kinase (1710 IU/L).	Agitation, Hallucinations, Psychosis, Prolonged behavioural disturbance, Reduced level of consciousness, Mydriasis.	Confusion, Hallucinations, Reduced level of consciousness Tachycardia (112/min), Clonus
Length of hospital stay (h)	133	44	6

160. First identification of the synthetic cannabinoid 5F-MDMB-PICA in Italy

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Objective: Synthetic cannabinoids (SCs) are the biggest group of novel psychoactive substances (NPS) monitored by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). Acute clinical manifestations vary and represent a challenge for clinicians. 5F-MDMB-PICA (or 5F-MDMB-2201) was first notified to the EMCCDA in September 2016 and toxicological data in humans are unavailable. We describe two analytically confirmed cases of 5F-MDMB-PICA intoxication, recently identified through the national emergency department (ED)-network referring to Pavia Poison Control Centre (PPCC).
Case series: Case 1 (July 2019). A 47-year-old male with positive history for psychiatric disorders and substance abuse (in therapy with citalopram and venlafaxine) was admitted to the ED with confusion, severe psychomotor agitation, tremors, mydriasis, tachycardia (116 bpm), bradypnea, and mild respiratory failure (oxygen saturation 89%). Blood analysis showed neutrophil leucocytosis, rhabdomyolysis and increase in C-reactive-protein, creatinine, AST, and troponin. He admitted consumption of a synthetic cathinone (eutylone). Immunoenzymatic urinary tests were positive for amphetamines and benzodiazepines. He was treated with fluids, benzodiazepines and transferred to a psychiatric ward two days later. Case 2 (September 2019). A 45-year-old man with positive history for substance abuse was brought to the ED with convulsions, hypotension, and respiratory acidosis (pH 7.24, pO_2 56, lactate 1.6). The clinical course was complicated by severe psychomotor agitation with purposeless and choreiform movements. He admitted consumption of an amphetamine-derivative sold on the Internet as O5O4FP (unobtainable product on the Web). Immunoenzymatic urinary tests were negative. He was discharged 36 hours later, after treatment with benzodiazepines. A plastic bag containing a light brown powder labelled "5F-MDMB-2201" made in the Netherlands was found at home. Urine, blood and product samples were analysed by chromatographic methods (GC-MS; LC-MS/MS, MRM operation mode) and 5F-MDMB-PICA was detected in blood from both patients (quantitative measurements are ongoing) and in the product (detected spectrum matched with the 5F-MDMB-2201 spectrum present both in electronic libraries (match quality 97%) and in literature data). Case 1 was also positive for eutylone in urine.
Conclusion: These cases confirm the presence of 5F-MDMB-PICA as NPS in Italy; our experience showed a prevalent neurotoxic effect with this compound. The association of more than one NPS complicates the clinical suspicion and may require a multidisciplinary medical approach. In these cases, laboratory support is essential to formulate the correct diagnosis. Clinical presentation of our patients without laboratory results could have required a complex pathway of differential diagnosis. The network between PPCC, toxicological laboratories and EDs inside the National Early Warning System plays a key role in early identification of NPS.

161. Severe drug intoxication in a specialized toxicology ICU - a retrospective study

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Objective: This report collects data from the Intensive Care Unit of our Clinical Toxicology Ward from 2010 to August 2019. The aim is to showcase the statistics of severe drug intoxications that needed ICU treatment, and the changes of frequency in the different substances.
Methods: Overall 85 cases were evaluated retrospectively and were analyzed in terms of gender, age, substance, toxicology laboratory results, duration of ICU treatment and complications.
Results: In total 85 patients were admitted to the Intensive Care Unit of our Clinical Toxicology ward, 17 females (20%) and 68 males (80%). The age ranged from 14 to 49 years, the average age was 29.2 years (24.0 years in women, 30.4 years in men). There were 7 fatal cases (8.2%), in 4 patients the substance was a new psychoactive substance (NPS; mephedrone or pentedrone), one case of heroin, one case of 3,4-methylenedioxymethamphetamine (MDMA) and one case of amphetamine intoxication were found. Three patients needed pre-hospital resuscitation. The cause of death was multi-organ failure in 6 patients. The average length of treatment was 3.6 days, and ranged from 1 to 29 days. There were 14 cases with complications without death; the most frequent (9 of 14) was pneumonia. The other 71 patients were discharged after they regained consciousness. In 12 cases (14.1%) more than one drug was used at the same time. Among the single substance cases, the most frequent was gamma-hydroxybutyrate (GHB) (34.3%). The highest GHB intoxication occurrence was seen in 2011 (9 patients were treated). As the number of NPS-intoxicated patients increased in the following years, the

incidence of GHB poisoning decreased. Amphetamine was steady with 1-4 cases per year and heroin almost disappeared. The toxicology samples were informative in 43 cases (50.6%). We were unable to detect GHB and synthetic cannabinoids, in these cases the patient's history and clinical symptoms aided the diagnosis.
Conclusion: In most cases, the prognosis of recreational drug intoxication is good, but severe intoxications can occur. Compared to the frequency of consumption, lethal cases are rare [1]. The most common substance was GHB, however the frequency started to decrease after 2011 and NPS intoxication started to increase. Although this data does not give an exact picture of drug poisoning incidence, it shows a tendency in the changes of the most commonly used substances.

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162. Arsenic exposure and peripheral neuropathy

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Objective: To determine the threshold concentration for the development of arsenic-induced peripheral neuropathy.
Methods: We conducted a systematic review of the literature to evaluate the relationship between arsenic concentrations and the development of peripheral neuropathy in humans. Two review authors independently searched "Medline" online database for case reports, observational studies and interventional trials which discussed arsenic and its potential to cause peripheral neuropathy. Titles and abstracts of all 61 papers were screened before conducting full-text reviews of successful papers. Strict inclusion and exclusion criteria were applied to select appropriate cases. We assessed the relationship between peripheral neuropathy and arsenic concentration in blood, spot urine and 24-hour urine data sets to identify a threshold exposure for arsenic-induced peripheral neuropathy. Data was analysed using descriptive statistics.
Results: We identified 16 studies reporting human arsenic exposure and peripheral neuropathy. The selected studies reported a total of 23 cases of arsenic poisoning. Fifteen cases reported spot urine arsenic concentrations, seven reported blood arsenic concentrations and six reported 24-hour urinary arsenic concentrations. Of the 23 cases of arsenic poisoning, 21 patients had peripheral neuropathy. The lowest arsenic concentration associated with peripheral neuropathy for blood was 20 µg/L, for spot urine 6 µg/L and 24-hour urine 441 µg/L. Establishing a Lowest Observed Adverse Effect Level (LOAEL) was not possible from the data obtained in this systematic review as there was no clear dose-response relationship between arsenic concentration and peripheral neuropathy. Explanations for this are likely to be multifactorial and include non-standardised diagnostic criteria resulting in cases of mild arsenic poisoning being misdiagnosed and thus under reported, variation in individual susceptibility to arsenic-induced peripheral neuropathy and, most importantly, inconsistent times between arsenic exposure and biomonitoring.
Conclusion: Making a diagnosis of arsenic-induced peripheral neuropathy is very challenging due to the extensive differential diagnoses. We identified the lowest arsenic concentration associated with peripheral neuropathy in the literature. This clinically relevant end point will aid clinicians investigating peripheral neuropathy; however, to identify a more accurate threshold concentration for arsenic-induced peripheral neuropathy, a prospective observational study may be required.

163. Gadolinum contrast media: old substance, new challenges

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Objective: Gadobutrol is a macrocyclic agent containing the heavy metal gadolinium. Clinical manifestations of gadolinium toxicity in patients with normal renal function are rare and we report a case.
Case report: A 44-year-old lactating woman without previous history of renal disease had magnetic resonance imaging (MRI) with gadobutrol for suspected gall bladder pathology. She interrupted breastfeeding for 24 hours following the MRI. That evening, she began to complain of chills, hot flashes, thirst, anxiety, rapid heartbeats, upper back pain, finger numbness, and muscle paresthesia (noted as twitching). She also reported severe insomnia, and was only able to sleep for approximately 4 hours every third day. She did not take sleeping pills because she continued breastfeeding. One month after exposure gadolinium concentrations were blood 2.203 µg/g of creatinine (reference range to 0.250 µg/g), urine 39.271 µg/L (reference range to 0.230), and breastmilk 0.214 µg/kg. Her renal function remained normal. Symptoms reduced in 2 months, but bone pain, numbness and paresthesia ("needles") of hands and feet remained. Moreover, she had tinnitus when she changed position. Chelation was not performed due to reduction in symptoms. Gadolinium concentrations in urine and blood will be repeated in 2 months for further analysis of the risk/benefit ratio of chelation therapy.
Conclusion: Gadolinium toxicity in this case varied from the acute adverse events to gadolinium deposition disease (GDD). Adverse events could be explained as an acute hypersensitivity reaction to gadolinium and starts from minutes to hours after administration. GDD is an immunological reaction to gadolinium deposition in tissues [1]. Whether the accumulated gadolinium is free Gd^{3+} or chelated gadolinium is not completely clear [2]. There are various studies that suggest the role of apoptosis, oxidative stress transmetallation, competition of Gd^{3+} with calcium ions for cellular processes and the release of chemokines and attraction of CD34+ fibrocytes [2]. Limited data exist about gadobutrol excretion in breastmilk and retention more than one day after the exposure. In rat studies less than 0.1% of the total administered dose was excreted in milk after intravenous injection [3]. Further analysis is needed for chronic gadolinium (free Gd^{3+} or chelated) toxicity for patients with normal renal function and for breastfeeding women.

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164. Case series of chronic occupational lead poisoning in shooting ranges

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Objective: Lead is widely regarded as an occupational health hazard [1], however, many employees working in high-risk environments, such as shooting ranges, still complain of lead poisoning-related symptoms. This may indicate a poor understanding of occupational safety, as well as lack of knowledge about the necessity of protective gear usage for employees working in lead-polluted environments. We describe a series of occupationally exposed workers with lead poisoning.
Case series: Five men whose age ranged from 32 to 57 years (mean 41.8 ± 10 years) were seen at the Toxicology Unit at the Republican Vilnius University Hospital, Lithuania, in the period 2016-2019. They complained of fatigue (5 patients out of 5), episodic dizziness (4/5), impaired memory (2/5), sleep disorders (2/5), distorted taste sensations (2/5), abdominal pain (1/5), impaired eyesight (1/5), paresthesia (1/5), rashes (1/5), heart palpitations (1/5), weight loss (1/5), a decrease in left arm muscle mass (1/5), decreased exercise tolerance (1/5), mood lability (1/5) and tinnitus (1/5). All of them were working as shooting instructors in indoor shooting ranges, with their work experience varying from 2 to 30 years. Clinical examination showed dangerously high blood lead concentrations, ranging from 304 to 458 µg/L (mean 387.2 ± 53.8 µg/L). Air lead concentrations were not measured at the shooting ranges they worked in.
Conclusion: Employees working at shooting ranges are highly vulnerable to daily lead exposure [2]. The highly elevated blood lead concentrations presented in the study indicate a lack of occupational health monitoring, as this was the first time any of the patients had had their blood lead concentration measured. This can also suggest a lack of knowledge about the dangers of lead poisoning, as some of the patients admitted not using recommended protective gear, e.g. dust masks or respirators.

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165. Comparison of unithiol (DMPS) treatment effect in two patients with severe cobalt intoxication

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Objective: Replacing a broken ceramic prosthesis with a cobalt-chromium prosthesis may lead to systemic intoxication, heart failure, transplant and even death. There is an urgent need to find the most efficient antidote for cobalt intoxication, however cases are limited and rarely described. We compare the only two patients in the literature treated with unithiol (dimercaptopropansulfonate, DMPS). It was successful for Patient 1 [1], and here we describe the course in Patient 2.
Case report: A 61-year-old male, had his damaged ceramic hip prosthesis replaced with a cobalt-chromium prosthesis in July 2015. In October 2016 he developed dislocation and deformation of this prosthesis, polyneuropathy, hypacusis, and hypothyreosis. In addition, severe non-ischemic cardiomyopathy was found with pericardial effusion and late gadolinium enhancement, necessitating implantation of a ventricular assist device. The cobalt serum concentration confirmed intoxication in 2018. The patient was treated with unithiol (400 mg/day) for 4 months; 13 serum and 14 urine samples were measured, with the lowest cobalt serum concentration after the heart transplant (Table 1). Leukopenia 1.9 × 10^9/L (reference 4.5-11.0 × 10^9/L) occurred as a side effect and due to requirement for immunosuppressants, the unithiol dosage was lowered and N-acetylcysteine (NAC) treatment will be considered until his hip revision and metal deposit debridement.
Conclusion: As removal of the prosthesis/metal deposit in the hip was not possible, the serum cobalt concentrations in Patient 2 remained elevated despite a higher urine output with the same unithiol dosage than in Patient 1. Removal of the heart with high

Table 1. Cobalt concentrations, history and outcome in two patients with cobalt-chromium prostheses.

	Time	Cobalt concentration in blood µg/L (± 30%)	Cobalt concentration in urine µg/L (± 30%)	Unithiol duration and dosage	Revision of the hip prosthesis	Heart transplant	Clinical outcome
Patient 1 [1]	Initially	506	139	1 month (10 g)	Provisional surgery and debridement	No	Almost completely recovered
	After one month of unithiol treatment	130	76.7		1.5 year later - final surgery		
	1.5 year later, before hip surgery	Not measured	25.7				
Patient 2	Pre-treatment improvement	92	Not measured	4 months (72 g)	Planned in November 2019	Yes July 2019	Minor
	After one month of treatment	86	121				
	After 4 months of unithiol	71	211				
	After heart transplant	53	Not measured				

a cobalt load decreased the cobalt concentration in the patient. (The cobalt concentration of heart tissue was 0.86 mg/kg and in controls was 0.05 mg/kg). Unithiol therapy probably prevented further elevations of serum cobalt before the two operations.

Acknowledgement

Progres Q25/1LF and Q29/1LF.

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166. Atypical mercury intoxication

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Objective: The National Toxicological Information Centre (NTIC) has consulted on several atypical mercury intoxications in previous years. For example the broken part of a mercury-containing thermometer in rectal muscle, inhalation and intravenous exposure as well as mercury exposure from a hand injury, as described here.
Case report: A 9-year-old boy was injured with a medical thermometer on the back of his hand in December, 2018. When shaking the thermometer, the mother accidentally injured the boýs hand. The minor laceration wound was treated at the surgery and the patient was prescribed antibiotics. On the 6th day after the injury, swelling of the hand and palm, redness and pain developed. Numbness in the fingers of the left hand was perceived by the patient. Tiny exanthema, which appeared predominantly on the abdomen and limbs, was probably an allergic reaction to mercury. The traumatologist assessed the condition as incipient phlegmon of the back of his left hand. The child was hospitalised. A computerised tomography (CT) scan displayed contrasting multiple opacities (6 x 4 mm) which also interfered with the deeper structures between the metacarpal III, IV diaphysis. The foreign bodies were surgically removed using X-ray. Biological material (urine, blood) was collected to determine the mercury concentration. The laboratory mercury standard is: blood <15.04 µg/L, urine 1.00-15.84 µg/L. Measured concentrations of mercury (14 December 2018, ten days after the injury) were: blood 11.63 µg/L and urine 28.08 µg/L. The child was treated with unithiol (dimercaptopropane sulfonate, DMPS) for 3 days. After antidote administration the concentration of mercury increased: blood 22.46 and then 29.28 µg/L, urine 134.59 and then 16.04 µg/L. For persistent elevated mercury values in biological material, unithiol treatment was repeated. After the second course of antidote the concentration of mercury decreased: blood 3.81 µg/L, urine 52.15 µg/L. The follow-up examination of biological material in January and May 2019 (after 1 and 5 months) was negative.
Conclusion: Mercury-containing measuring devices have been used for many years in households but European legislation on chemicals led to a ban on the sale of mercury-containing thermometers to the general public in April 2009. We would like to stress, that even in mercury innocent-looking cases, a X-ray/CT examination should be used.

167. Iron overdose in pregnancy

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Objective: Acute iron overdose in pregnancy can be fatal, and stage 3 toxicity can be associated with adverse perinatal outcome [1]. The use of deferoxamine, a potent iron chelator, is often withheld in pregnant women on the basis of theoretical fetal effect, although, it would be indicated. We report a case of acute self-poisoning, which was managed with deferoxamine without adverse consequences.
Case report: A 30-year-old, 26 weeks gravida ingested 50 tablets of Neo-Ferro-Folgamma (each tablet contains 37 mg elemental iron, total dose 20.8 mg/kg elemental iron). A few hours after ingestion she developed nausea, continuous vomiting and intense abdominal cramps. On admission her physical status was satisfying, and fetal evaluation by ultrasound was normal. The patient's laboratory results included an initial serum iron concentration of 93.0 µmol/L (4 hours after ingestion), and peak serum iron concentration of 118.0 µmol/L (normal 10-28 µmol/L). Her electrolytes, liver enzymes and renal function tests were all within the normal ranges. Four hours after ingestion gastric lavage was performed, then whole bowel irrigation was started, and she was treated with supportive care. Deferoxamine therapy is indicated for individuals with symptoms, and for those ingesting more than 20 mg/kg elemental iron or serum iron concentration more than 90 µmol/L. Based on these criteria we began deferoxamine therapy (15 mg/kg/h intravenously) . The patient tolerated it well. Deferoxamine was continued until symptoms resolved, serum iron concentration returned to a normal range, and vin rose coloration of urine was cleared. The total duration of deferoxamine therapy was 20 hours. During her observation we could detect only mildly low INR and mildly elevated alkaline phosphatase. She was discharged on hospital day 5. At home she was checked by a gynecologist, her pregnancy continued normally, and she delivered a healthy baby at term.
Conclusion: Acute iron intoxication can cause multi-organ complications and can be fatal. Treatment is well-defined, based on the patient's symptoms, amount of elemental iron consumed and serum iron concentration. In this case we treated a pregnant iron-intoxicated woman with appropriate supportive care, effective early decontamination and chelation (deferoxamine) therapy. Deferoxamine was given intravenously with no side effects. Our patient did not develop any lasting consequences of the overdose or treatment. In this case deferoxamine was safe and effective in late pregnancy.

Reference

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168. Toxicokinetics of silver and unithiol (DMPS) chelation challenge tests in argyria due to colloidal silver

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Objective: Argyria is benign grey discolouration of the skin from exposure to silver. Management is limited to discontinuation of the use of silver; chelation is not recommended. We report a toxicokinetic study of silver and unithiol (2,3-dimercapto-1-propane sulfonate, DMPS) challenge tests in the patient with argyria due to colloidal silver ingestion.
Case report: A 39-year-old man with a history of alcohol abuse was admitted due to bluish skin and greyish hair discoloration and fine tremor. He reported drinking 100-500 mL of colloidal silver daily for 6 months to regenerate body cells. He was buying colloidal silver on the Internet (30 EUR/500 mL bottle). Colloidal silver bottles were labelled to contain 12 ppm of silver (12 mg/L), but measured silver level in the bottle that he brought with him was 17 mg/L. An estimated dose of ingested silver over 6 months was 300-1500 mg. Laboratory investigations using inductively coupled plasma mass spectrometry showed more than 60-fold increased serum concentration of silver (18.18 µg/L; reference <0.28 µg/L) and a random urine silver/creatinine ratio of 0.282 µg/g (urine silver concentration 0.571 µg/L). Skin biopsy confirmed silver deposits around basement membrane of the eccrine sweat glands. Electromyography was normal. The patient was advised to discontinue use of the solution. Two and 6 weeks later serum silver serum concentrations decreased to 5.50 µg/L and 1.03 µg/L, respectively; however, no visible skin colour improvement was noted. At 6 weeks 300 mg unithiol-silver challenge tests showed a 12-fold increase in silver urine excretion (urine silver/creatinine ratio before unithiol was 0.028 µg/g and after unithiol 0.340 µg/g). Chelation therapy was not introduced, since measured daily urine excretion of silver after unithiol was only 1.5 µg/day representing one millionth of the ingested dose. Follow-up at 16 weeks revealed further decrease of serum silver concentration (0.65 µg/L) and slight improvement of bluish skin discoloration according to subjective assessment by the patient. Toxicokinetic analysis of the measured serum silver concentrations was performed and revealed elimination half-life of 9 days during the first 6 weeks.
Conclusion: Ingestion of 300-1500 mg of colloidal silver over 6 months can result in elevated serum silver concentrations and mild argyria. Serum silver elimination half-life is 9 days during the first weeks after cessation with colloidal silver. Unithiol increases daily urinary excretion by a factor of 12, but chelation therapy is not clinically relevant. Physicians and natural healers should be aware that patients consuming silver-containing solutions are at risk of argyria.

170. Persistent arsenic toxic encephalopathy associated with negative neuroimaging in an elderly male

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Objective: Arsenic toxicity associated with encephalopathy is often associated with abnormal magnetic resonance imaging (MRI) findings. We present a fatal case of arsenic toxicity associated with prolonged encephalopathy in the absence of abnormal MRI findings.
Case report: A 72-year old man was referred to an emergency department with two weeks of ataxia, otalgia, and bilateral hearing loss after his primary care physician noted an elevated spot urine arsenic concentration of >50 µg/L. The patient denied well-water, working with metals, recent seafood consumption, or known exposure to arsenic. Upon admission he was noted to also have Mee's lines on his fingernails as well as a keratotic rash on his hands. His whole blood inorganic arsenic concentration was 27 µg/L and organic concentration was 10 µg/L. His arsenic/creatinine ratio was 12. The patient initially left the hospital after becoming agitated with staff but returned three days later with worsening symptoms. Dimercaprol (British anti-Lewisite, BAL) was initiated as succimer (dimercaptosuccinic acid, DMSA) was unavailable. He was given antipsychotics and benzodiazepines on day two due to increased agitation as dimercaprol was continued for 5 days. On day 6 he developed hypoxia and pulmonary infiltrates consistent with pneumonia and required intubation. On day 12 a 24-hour urine and whole blood arsenic concentrations were undetectable. An MRI on day 19 did not show cerebral edema, increased T2-flair signals or other abnormalities. He remained comatose and critically ill and died of cardiopulmonary arrest on day 42.
Conclusion: Toxic encephalopathy associated with arsenic toxicity has been reported and is frequently associated with changes in MRI. Specific acute changes include cerebral edema as well as increased T2-flair signal on MRI. Additionally, cortical atrophy has been reported to present in a delayed manner 1-6 months after exposure [1]. The absence of MRI findings associated with prolonged and severe coma in the setting of arsenic toxicity should not preclude aggressive treatment with chelation and supportive care.

Reference

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171. Accidental ingestion of sodium nitrite with lethal outcome

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Objective: Sodium nitrite is a highly toxic and widely used potent oxidizer, and accidental and intentional poisonings are described. We report a lethal poisoning.
Case report: A 66-year-old man working at a timber processing company drank a mouthful from a presumed water bottle. Noticing a strange taste, he tried to induce vomiting without success. Thirty minutes later he developed nausea, pale skin and had an episode of syncope. His blood pressure (BP) was 71/47 mmHg, the radial pulse barely palpable, and his oxygen saturation 90%. His degree of consciousness decreased. Upon arrival

at the hospital 90 minutes post-ingestion he was cyanotic with BP 80/40 mmHg, Glasgow Coma Score (GCS) 3, heart rate 65/min and respiratory rate 30/min. SpO_2 was 83% while arterial pO_2 was 14.8 kPa (on oxygen). His blood had a coffee-brown color. Arterial blood gas analysis showed lactic acidosis (lactate 12.9 mmol/L) with base deficit (15.2 mmol/L). Methemoglobin was confirmed, but could not be quantified. Cyanosis, brownish colored blood and normal pO_2 combined with low SpO_2 on pulse oximeter are highly suggestive of methemoglobinemia [1]. Sodium nitrite is used at the patient's workplace and was suspected as the ingested substance due to the clinical picture with hypotension and methemoglobinemia. The patient was intubated and treated with vasopressors. Methylene blue was not available, and he was considered too unstable for transport. Instead, an attempt was made to obtain methylene blue by helicopter as response to symptomatic treatment was poor. The patient's condition deteriorated, with bradycardia, hypotension and further decrease in oxygen saturation. Two hours after the ingestion he had a cardiac arrest and died. Autopsy findings were consistent with nitrite poisoning. The concentration of sodium nitrite in the ingested fluid was specified by the workplace to be 420 g/L, and the estimated amount ingested was 20-30 g. The employer later accepted a fine for inadequate procedures in handling and labeling of hazardous chemicals.

Conclusion: The lethal dose of sodium nitrite in humans is not well established but death is reported after ingestion of 1 g [2]. Ingestion of a concentrated solution of sodium nitrite can be lethal even if only a small volume is ingested. Safe handling and storage of such potent chemicals is crucial to avoiding accidental poisoning.

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172. Spanish Toxic Surveillance System (STSS): occupational exposures in a two-year period

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Objective: Since 1999, a Toxicosurveillance System exists in Spain promoted by the Spanish Ministry of Health and implemented by members of the Spanish Foundation on Clinical Toxicology. The system aims to report cases of acute poisoning by chemical products admitted to the Emergency Department (ED) of selected hospitals to evaluate the risks of exposure to these substances under current EU regulations. The register analyses the main circumstances leading to chemical exposure, including those of occupational origin. We present the characteristics of these occupational exposures in the last two-year period.

Methods: The participating hospitals report all cases of intoxication due to household, agricultural or industrial chemicals treated in their ED by means of an online 24 hour accessible encrypted questionnaire. A yearly report is presented to the Health Ministry. We have selected the occupational cases gathered by the system from the 23 participant hospitals, covering a population of about 10 million people, between January 2017 and December 2018. The analysed variables were age, sex, day and month, type of chemical, route of entry, symptoms, treatment and evolution.

Results: We collected 201 occupational cases. Median patient age was 40 ± 11 years. Distribution by sex was 148 men (74%) and 53 women (26%). The main routes of entry were respiratory (71%) and ocular (22%). Cutaneous contact (8%) and oral (5%) were much less frequent. The main chemicals involved were carbon monoxide (28%), irritant gases (22%), solvents (11%), and caustics (8%). Overall 91% of the patients were symptomatic at admission presenting with respiratory (36%), neurological (32%), ocular (25%), digestive (20%), and cutaneous (9%) symptoms, most of them mild. Symptomatic treatment was given in 82% of the cases. Ocular/cutaneous decontamination was used in 29%. In 25% of the cases, oxygen was used as an antidote for carbon monoxide exposure. Only 16 cases required hospital admission, two of them in the intensive care unit. Sequelae occurred in 11 cases and were mainly due to hydrogen sulphide and chlorine exposure. No deaths were recorded.

Conclusion: The STSS proves to be a useful tool for keeping an accurate register of incidents related to patients with chemical exposures attending EDs. Occupational toxic exposures in Spain are currently rare and with mild consequences. The main hazardous classical chemicals, such as heavy metals or pesticides, do not appear in our series, which proves the success of the regulatory preventive rules implemented over the last few decades under EU regulations.

173. Spanish Toxic Surveillance System (STSS): comparison of occupational and non-occupational exposures in a two-year period

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Objective: Since 1999, a Toxicosurveillance System exists in Spain promoted by the Spanish Ministry of Health and implemented by members of the Spanish Foundation on Clinical Toxicology. The system aims to report cases of acute poisoning by chemical products admitted in the emergency department (ED) of selected hospitals to evaluate the risks of exposure to these substances under current EU regulations. The register analyses the main circumstances leading to chemical exposure, including those of occupational origin. We compare the characteristics of occupational with non-occupational exposures in the last two-year period.

Methods: We selected the occupational cases gathered by the system between January 2017 and December 2018. We compared some of the variables (age, sex, type of chemical, route of entry, symptoms, treatment and evolution) looking for differences between occupational and non-occupational chemical exposure.

Statistical signification of qualitative variables ($p < 0.05$) was found by means of chi-square test.
Results: From the 2290 registered cases, 201 were occupational. Most cases involved domestic accidents (78%). The comparative analysis shows the following results: mean age of occupational cases (41 ± 11 years old) was slightly over the non-occupational group (38 ± 24 years old) due to the absence of children. Men were overrepresented (70%) in the occupational group ($p < 0.001$) versus an even sex distribution in the non-occupational group. The main chemicals in the occupational cases were toxic (30%) and irritant (28%) gases while, in the non-occupational group, caustics were the second involved substances (18%) following toxic gases. Respiratory (68%) ($p = 0.04$), ocular (21%) ($p = 0.037$) and cutaneous (8%) ($p < 0.001$) routes of exposure predominated in the occupational cases, while, in the non-occupational group, oral (35%) was the second most common route after inhalation. Respiratory, ocular and cutaneous symptoms were more prevalent in occupational cases ($p < 0.001$). Antidotes and cutaneous decontamination were more frequently used in occupational cases ($p < 0.001$), while gastric decontamination was more prevalent in non-occupational exposures ($p = 0.022$). Hospital admission was less frequent in occupational cases (8%) than non-occupational cases (15%) ($p = 0.006$).
Conclusion: There are relevant differences between occupational and non-occupational cases of chemical exposure. Occupational cases present in a slightly older population, with a clear male predominance. Toxic and irritant gases and solvents are more prevalent in occupational cases. Occupational cases show a better outcome with less of them requiring hospital admission and no mortality.

174. Osmium tetroxide: rare ocular and dermal exposure

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Objective: Osmium tetroxide (OsO_4), an oxidation product of osmium metal, is a strong oxidizing agent and may cause severe burns to the eyes (including irreversible blindness), and damage to the skin, respiratory and gastrointestinal tracts. The toxic and lethal human dose has not been delineated. We describe a case of very rare ocular and dermal damage by osmium tetroxide.
Case report: A 32-year-old woman was admitted to hospital in January 2019 about 30 minutes after she spilled the content of a 9 mL glass ampule of 2% OsO_4 in acetone on her skin at her workplace. The spill included her left eye, left hand, upper back, and neck. Immediately after exposure she felt burning of the eyes and had lacrimation. Additionally, painless grey spots appeared on the affected skin. She started to rinse her eyes immediately and washed her skin with water for about 7 minutes. Ophthalmological examination revealed grey dots and small erosions of her left cornea. Local eye therapy combining antibiotics, corticosteroids and dexpanthenol gel (5%) for soothing the cornea was started and applied for one week. Some improvement was seen on the next day, and gradually, the cornea lost its greyness and within 10 days after exposure all spots disappeared, and the cornea became transparent. Fourteen dark grey spots on her skin (0.5 cm in diameter) disappeared within 14 days. She was hospitalized for 24 hours, rehydrated, and followed for one month. Osmium serum level was 0.22 µg/L 19 hours after exposure. Osmium concentrations in three spot urine samples collected over 15 hours were 7.05 µg/L; 1.65 µg/L, and 8.45 µg/L. The biochemical analysis on admission, one and two weeks later showed elevated concentrations of serum iron (28.2 µmol/L, 39.8 µmol/L, and 50.5 µmol/L (reference range 5.8-34.5 µmol/L and transferrin 1.6 µmol/L, and 2.5 µmol/L (reference range 2.0-3.0 µmol/L) with normal blood count but returned to reference ranges within one month. Other possible causes were excluded. The patient recovered completely within four weeks.
Conclusion: Since exposure to osmium and its compounds are extremely rare, valuable information is obtained with every case report. Fast and prolonged first aid may prevent irreversible damage. Osmium urine concentrations proved significant absorption from the skin, and potentially from the eyes. Iron and transferrin elevations after osmium tetroxide exposure have not previously been described; and a causal relationship remains questionable.

Acknowledgement

Progres Q25/1LF and Q29/1LF.

175. EXP3OP study: occupational eye exposures reported to a western France poison center

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Objective: Eye burns in the workplace are frequent and potentially severe, sometimes resulting in irreversible damage. The objective of this study is to describe the epidemiological trends, prevention and management measures implemented in the context of occupational eye exposures in order to improve prevention measures in the workplace.
Methods: This is a prospective descriptive study carried out over a period of 3 months of cases of eye exposure in the context of an occupational activity, reported at the Angers Poison Control Center (PCC). The data were collected during telephone consultations with the Angers PCC.
Results: Between 1 October 2018 and 31 December 2018, 178 patients with occupational eye exposure were identified. The sex ratio (M/F) was 1.9. The median age was 34 years. The most affected age groups were 20-29 years old (25% for women, 24.5% for men) and 30-39 years old (24.5% for both men and women). The occupations most at risk were building trade/mechanics/plumbing (15.5%), agriculture (11.8%) and cleaning industry (11.1%). Alkaline agents were most frequently involved (32.1% of cases), followed by acids (17%) and detergents (13.2%). The severity of eye damage, assessed according to the Poison Severity Score (PSS), was distributed as follows: PSS0/1 72% and PSS2/3 28%. Alkaline exposures were associated with higher severity ($p < 0.05$). Thirteen patients had severe eye damage (corneal ulcer, perforation) and two of them were hospitalized. The patients in the study were on medical leave in 33.9% of cases, with an average duration of 5.4 days. Less than half of the patients (46.7%) had been offered personal protective equipment by their employer. Of these, only 37.9% were equipped with them at the time of the accident.
Conclusion: Chemical eye burns are common in the workplace, with products that are often dangerous and highly concentrated. Strict preventive measures and a standardized management protocol are essential in order to prevent severe complications that can have a significant functional impact (visual acuity, pain, ophthalmological complications) and social impact (hospitalization, sick leave).

176. Lab mistake causes mustard gas exposure

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Objective: Sulfur mustard, also known as mustard gas, a highly toxic, vesicant warfare agent, in pure form is a colourless to yellow oily liquid. Due to its decomposition products or byproducts, it has a horseradish or garlic-like odour. The compound is very hydrophobic and is absorbed percutaneously, via mucous membranes or by inhalation. Depending on concentration, exposure duration and localisation, severe painful lesions of tissue may appear. Full clinical symptoms emerge with a latency period of hours to days. Furthermore, mustard gas is carcinogenic and can cause bone marrow suppression [1–3]. We report exposure following a laboratory accident.
Case report: During a routine laboratory microwave operation, a food chemist intended to suspend a batch of samples in 0.1 mol/L hydrochloric acid in a hot atmosphere of 6 mol/L hydrochloric acid. Confusing chemicals, she accidentally used a 2% thiodiglycol solution instead of the higher concentrated hydrochloric acid. Opening the microwave, she noticed a garlic-like odour. Although she placed the samples immediately under the hood, she experienced a brief exposure to the chemical. Having left the laboratory, she washed her face and hands with water. She instantly showed symptoms of perioral paresthesia and burning of her upper lip, later on a general malaise, headache and foreign body sensations in her eyes and nose occurred. She contacted a hospital 3.5 hours after exposure. In the further course, small blisters appeared on her upper lip and on her left index finger, persisting for a few days. The laboratory analysis for albumin adducts was negative.
Conclusion: The formation of sulfur mustard by using thiodiglycol as a chemical agent usually requires concentrated hydrochloric acid (Meyer-Clarke method), but this case suggests that the heat of the microwave may have favored the reaction. Moreover, exposure to so-called potential warfare agents may also occur out of a military context. We highly recommend that in future cases institutes of pharmacology and toxicology and facilities of military medicine are involved in such cases.

References

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177. What may proteomics say about occupational nano-exposure?

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Objective: Thousands of employees worldwide work in nanocomposite manufacturing, and oxidative stress markers in their biological fluids have been found in initial studies. Yet little is

Table 1. Proteins and their genes according to the Human Protein Atlas [1].

Protein		Gene	Classification related to diseases	Organ of origin of the protein
Higher concentration in nano-exposed workers				
1	Fibrinogen alpha chain receptor	FGA	Cancer-related genes, candidate cardiovascular disease genes, disease related genes	Liver
2	Complement C3	C3	Candidate cardiovascular disease genes, disease related genes	Liver
3	Ig mu chain C region	IGHM	Disease related genes	Testis
4	Mucin-5B	MUC5B	Disease related genes	Nasopharynx, bronchus, gastrointestinal tract, gall bladder, bone marrow
5	Glycosylasparaginase	AGA	Disease related genes	Parathyroid and adrenal gland, gastrointestinal tract, gall bladder, pancreas, kidney, testis, prostate, seminal vesicle
6	Deleted in malignant brain tumours 1 protein	DMBT1	–	Gastrointestinal tract
7	Polymeric immunoglobulin receptor	PIGR	Cancer-related genes	Nasopharynx, bronchus, gastrointestinal tract, gall bladder, kidney, urinary bladder, endometrium, cervix
8	Fibrinogen beta chain	FGB	Cancer-related genes and candidate cardiovascular disease genes	Liver
9	Ubiquitin	UBA52		All organs
10	Annexin A7	ANXA7	Cancer-related genes	Most organs
11	Catalase	CAT	Cancer-related genes, disease related genes	Liver
12	Apolipoprotein A-I	APOA1	Cancer-related genes, candidate cardiovascular disease genes, disease related genes	Liver and gall bladder
Lower concentration in nano-exposed workers				
1	WAP four-disulfide core domain protein 12	FWDC12	–	Male tissues, skin
2	BPI fold-containing family B member 1	BPIFB1	–	Bronchus, cervix
3	Serotransferrin	TF	Cancer-related genes, disease related genes	Liver

known about the potential health consequences. This pilot study used untargeted proteomic analysis of exhaled breath condensate (EBC) to estimate effects of nanoparticle exposure.
Methods: Aerosol exposures were monitored during nanoparticle generation operations: smelting, welding and nanocomposites machining, using a suite of real-time and integrated instruments. EBC was collected from 10 exposed subjects (42.8 ± 11.0 years, 8 males/2 females), and 21 controls (41.6 ± 6.7 years, 17 males/4 females). The shotgun method for identifying proteins was performed after proteolytic digestion and high-performance liquid chromatography combined with mass spectrometry. Raw data was evaluated using MaxQuant software and the Human Protein Atlas [1].
Results: Aerosol mass concentration ranged from 0.120 mg/m^3 to 1.840 mg/m^3 during nanocomposite processing; median particle number concentration was 4.8x10^4 to 5.4x10^5 particles/cm^3. The proportion of nanoparticles was 40-95%. Among 414 proteins detected in both groups, 28 proteins were expressed differently in the group exposed to nanoparticles compared to controls ($p<0.05$). Twenty-three proteins had at a higher concentration, another 5 proteins a lower concentration. When proteins with limited data in the Human Protein Atlas and those originating in the salivary gland were excluded as potential contaminants, 15 proteins remained (Table 1). In addition, superoxide dismutase was non-significantly lower ($p = 0.086$)
Conclusion: Pilot data show that 75% of proteins with a higher concentration were classified as related to diseases, and only 33% of proteins with a lower concentration were disease-related. Proteomics of EBC may point to the mechanisms of action of nanoparticles.

Acknowledgement

GACR 18-02079S, Progres Q25/1LF and Q29/1LF.

Reference

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178. The role of CYP450 in the molecular toxicology of sulfur mustard *in vitro*

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Objective: Sulfur mustard (SM) is a banned chemical warfare agent (CWA) that still poses a threat to public safety due to its easy production and the recent use as a CWA (e.g. Syria crisis). Despite years of research, the molecular toxicology of SM is still not completely elucidated and further research is needed to find appropriate causal therapies. Oxidation processes of SM seem inevitable after entry into the organism and it is already known that SM is metabolized by oxidative processes. The aim of our study was therefore the comparison of the cytotoxicity between SM itself and its oxidation products sulfur mustard sulfoxide (SMO), sulfur mustard sulfone (SMO_2) and divinyl sulfone (DVS) *in vitro*. Moreover, we investigated the role of CYP450 in that process, whereby CYP1A2 was taken as a model for analyzing the role of CYP450 enzymes in SM poisoning.
Methods: Cytotoxicity of SM or its oxidation products SMO, SMO_2, and DVS in HepG2 cells was determined under basal conditions and after modulation of CYP1A2 activity (induction and inhibition) using the viability assay XTT. Western blot analysis was used to verify the expression of CYP1A2 in HepG2 cells. Activity of CYP1A2 was analyzed under basal conditions and after induction and inhibition with 100 µM omeprazole and 5 mM cimetidine, respectively, using special P450-Glo assays.
Results: Comparison of the cytotoxicity between SM itself and its oxidation products revealed a significant higher toxicity of SMO_2 and DVS ($LC_{50} \sim 15$ µM) compared to SM ($LC_{50} \sim 36$ µM) while SMO had no effect at any concentration. Both, induction and inhibition of CYP1A2 in HepG2 resulted in significant changes in cytotoxicity after exposure. Induction of CYP1A2 with omeprazole led to a decreased cytotoxicity for all compounds ($LC_{50} \sim$ 66-104 µM) whereas inhibition with cimetidine resulted in an increased cytotoxicity for SM ($LC_{50} \sim 25$ µM), but not for SMO_2 and DVS.
Conclusion: Modulation of CYP1A2 activity affected cytotoxicity in HepG2 cells significantly. Thus, CYP450 plays a pivotal role in the metabolism of SM, SMO_2 and DVS. Especially CYP1A2 induction with omeprazole decreased the toxicity *in vitro*. The presented findings are an important step in gaining more insight into the complex metabolism of SM and could contribute to treatment of victims of SM-poisoning e.g. by developing useful co-medications with the CYP-inductor omeprazole. Future studies should now address the metabolic conversion of SM in more detail.

179. Human skin explants *ex vivo* study: lesions caused by topical exposure to 25% tetramethylammonium hydroxide (TMAH)

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Objective: Tetramethylammonium hydroxide (TMAH) is a quaternary ammonium compound and strong corrosive base. It dissociates into TMA^+ and OH^- ions, causing chemical skin/eye injuries and sometimes fatal systemic toxicity. Dermal injury from the OH^- ion may increase TMA^+ tissue penetration. This study was performed to evaluate general morphology effects of TMAH contamination on human skin explants *ex vivo*.
Methods: With informed consent, 60 human skin explants were prepared from an abdominoplasty sample and preserved *ex vivo* in BIO-EC's Explant Medium at 37 °C in a humid atmosphere containing 5% CO_2. Explants were divided into 13 groups for a range-finding study: (1) untreated controls, (2-13) as follows: there were explants exposed to 2.5% TMAH (4 groups), 5% TMAH (4 group), or 25% TMAH (4 groups). Explants were exposed to 25% TMAH solution for different time periods 1, 5, 10, and 20 minutes, 1, 2, 4, 8, and 24 hours. TMAH was applied on a 9 mm filter paper saturated with 30 µL. Duplicate explant samples were taken from all groups on Day 0, and compared with triplicate samples from all groups at 24 hours post-exposure. Samples were either fixed in buffered formol or preserved frozen at -80 °C. Samples were prepared for histological evaluation.

Sample preparation: dehydration and impregnation into paraffin using a Leica PEARL automatic dehydrator, then cut into blocks with a Leica EG 1160 coating station. Then 5 µm slices were prepared with a Leica RM Minot-type microtome and mounted on glass Superfrost® slides. Slides were stained with the Goldner variant of Masson's Trichrome. Optical microscopy was performed with a Leica-type DML-B or Olympus BX42. Photomicrographs were taken with an Olympus DLP72 and Cell software.
Results: After a 25% TMAH contact time of 1 hour, the general morphology of the epidermis and dermis were totally altered. With longer contact times, 2 of 3 explants were very significantly altered, however, alterations were irregular (2 of 3 explants). Alterations were observed at 24 hours after a 20 minute contact time.
Conclusion: Based on these results, for future studies in this model, a 25% TMAH solution contact time appears to be the best option and >3 samples could minimize possible sample heterogenicity.

181. "All right, I'll be more careful next time": frequent callers in Finnish Poison Information Centre (FPIC)

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Objective: The purpose was to study the call patterns of frequent callers to the Finnish Poison Information Centre (FPIC).
Methods: FPIC call records from 1 January 2010 to 31 August 2019 were studied (n = 361,761). Index terms searched were "regular", "frequent", "before", "previously" and by known names and hometowns of the frequent callers. A frequent caller is an individual, who repeatedly calls our center. Records from the frequent callers were included for further study (n = 1451). In addition, the calls of a caller named "X" were examined more closely.
Results: The average percentage of these frequent calls was 0.4%/year (range 0.1-1.0%). These callers can represent approximately 0.01% of all inhabitants in the caller's hometown but can make up to 92% of all calls. For example, in town A, over a period of 4 years, one caller made 5-92% of the yearly calls from that region. In town B, over a period of 2 months another caller made 34-64% of the monthly calls. In large cities, the percentages are small in relation to population. We noted no difference in genders. The age of frequent callers was 25-45 years. Case example: Caller X has been calling to us for 9 years (about 600 calls, overall). X lives in a small town and X's calls have amounted to 6-44% of the calls from that region. X has medication, which X usually takes "one pill too many by accident". X´s questions concern mainly citalopram and comprise 3-61%/year of the all annual calls related to citalopram, propranolol (1-27%/year) and methylphenidate (1-15%/year). There are study limitations. We cannot detect every call from the frequent callers. We do not have any official recognizing system for these callers, so the exact number of individual callers remains undetermined.
Conclusion: Although frequent callers make up a small percentage of our total calls, they can temporarily burden our call center. The amount of calls, especially for citalopram, changes the relationship to real events and thus distorts our statistics. These calls can show the lack of a caller's safety net in primary healthcare. This is a common phenomenon with healthcare telephone services and we must just handle them one call at a time.

183. Extracorporeal membrane oxygenation (ECMO) in severe drug intoxication: a retrospective cohort study of 17 cases

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Objective: In toxicological refractory circulatory failure, use of extracorporeal membrane oxygenation (ECMO) could be an option. The aim of this report was to present the results of ECMO in this setting and to identify factors associated with hospital mortality.
Methods: Retrospective cohort study of all consecutive patients who received ECMO for refractory shock or refractory cardiac arrest following drug intoxication in our intensive care unit (ICU), 2014-2018. Survival rate and the Cerebral Performance Categories (CPC) score were ascertained on ICU discharge. Baselines at the time of ECMO initiation were compared between groups (survivors and non-survivors) using Fisher's exact 2 test for qualitative variables and using the Mann-Whitney test for continuous variables. All tests were two-sided, and a p value less than 0.05 was considered statistically significant.
Results: In total 9181 patients were admitted for drug intoxication in the study period, with 200 patients with hemodynamic failure responding to conventional treatment and 17 patients treated with ECMO. Eight patients were treated with ECMO for refractory shock (survival rate with CPC 1 75%, n = 6/8) and nine for refractory cardiac arrest (survival rate with CPC 1 33.3%, n = 3/9). At the time of ECMO initiation, mortality and poor neurologic outcome (CPC 4) were associated with high lactate concentration (p < 0.0001), low bicarbonate concentration and low pH blood levels (p = 0.04 and 0.03 respectively), elevated troponin concentration (p = 0.04), and more severe prognostic scores (Simplified Acute Physiology Score (SAPS) II, Sequential Organ Failure Assessment (SOFA) and Survival After Veno-arterial ECMO (SAVE) score; p < 0.01). In refractory cardiac arrest, low-flow time was significantly higher in non-survivors and CPC 4 patients (p = 0.04). No patient with lactate level above 9 mmol/L, SAPS II score above 80 and low-flow time above 60 minutes before ECMO implantation survived with good neurologic outcomes.
Conclusion: ECMO could be an attractive emergency resuscitative tool in highly selected poisoned patients who do not respond to conventional therapies. Further studies are needed to clarify prognostic factors of drug poisonings and, therefore, the indications and usefulness of peripheral ECMO.
Trial registration. This database was registered at the Commission Nationale de l'Informatique et des Libertés (CNIL, registration no. DEC18-348).

184. Risky dietary supplements: self-harm with potassium salt capsules

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Objective: Hypokalemia in Sweden is usually only seen in patients with eating disorders, kidney-related diseases and those treated with diuretics. The most common treatment is modified-release tablets that release potassium chloride throughout the

Table 1. Patient details and potassium concentration after overdose with over-the-counter (OTC) potassium supplements.

Sex	Age (years)	Stated amount ingested	Blood potassium concentration (mmol/L)	Time post-ingestion
F	23	50 × 288 mg	8.0	1.5 h
F	27	90 × 288 mg	7.2	1.5 h
F	Adult	100 × 255 mg	8.8	1.5 h
F	38	Unknown	6.1	1.0 h

gastrointestinal tract over 6-8 hours. Overdoses are often complicated by bezoar formation with symptomatic latency and multiphasic release over extended periods of time. In 2012 the European Commission permitted the use of health claims regarding potassium in the maintenance of normal blood pressure, and nerve and muscle function [1]. With this decision several OTC dietary supplements containing potassium salts have appeared on the Swedish market.

Methods: The case records of the Swedish Poison Information Centre were searched for cases of overdosing OTC potassium supplements between January 2015 and September 2019.

Results: Nine cases of potassium overdose, all of them due to intentional self-harm, were identified. Four cases could be evaluated based on information about potassium concentration and time of ingestion, while five cases lacked follow-up information. All cases involved products containing potassium salts with high solubility such as citrate or gluconate. Rapid and complete absorption lead to high concentrations within 1-2 hours. The patients were treated with glucose-insulin infusion. No rebound hyperkalemia occurred and all patients made complete recoveries.

Conclusion: Dietary potassium supplements can cause life-threatening hyperkalemia when taken in overdose. The products usually contain soluble salts which together with the almost complete absorption of potassium can lead to rapid onset of symptoms, in contrast to the modified-release formulations commonly used in the clinical management of hypokalemia.

Reference

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185. Valproic acid in the management of delirious, agitated critically ill toxicology patients

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Objective: Delirium is a frequent complication of severe poisoning and critical care methods involved in management of poisoning. Valproic acid (VPA), an anticonvulsant with distinct mechanisms of action, is a potential adjunct to standard sedatives in "refractory hyperactive delirium" [1]. We report VPA used in the management of poisoned patients with delirium and agitation in the intensive care unit (ICU).

Case series: Patients came to the attention of the Consultation-Liaison Psychiatry service after admission to the ICU for severe agitation deemed secondary to intoxication and/or withdrawal. Patients received VPA if they had been treated with dexmedetomidine, propofol, midazolam, and haloperidol and/or olanzapine without achieving adequate sedation and progressing toward extubation by the fifth day of admission. Seven of the 9 patients were men aged 20-42.8 years. Patients were given parenteral ketamine (2-5 mg/kg) initially. Exposure to methamphetamines and cocaine was confirmed in seven and two patients, respectively. Four reported consumption of a synthetic cannabinoid and two were suspected of using a synthetic stimulant. Confirmatory toxicologic testing was not available for novel substances. Five patients had confirmed ethanol consumption. There were documented histories of post-traumatic stress disorder (PTSD) and antisocial personality disorder in 6 and 4 patients, respectively. Doses of VPA were employed above that based on standard pharmacokinetics (range 3500-7000 mg IV/day, in 4 divided doses) and serum concentrations guided dosing, with a target range of 70-120 mg/L. Levocarnitine was given empirically (500-1000 mg IV 3 times daily) to support safe metabolism. The other active sedative treatments above were continued initially, with preference given to discontinue olanzapine first, then propofol, then benzodiazepines as effects of VPA were realized. Patients displayed less agitation as measured by the Richmond Agitation and Sedation Scale (RASS) an average of 42 hours after initiation of VPA (range 16-108 hours). Average RASS on the day of initiation of VPA was 3.1, decreasing to 1.2 two days later. Prior to this series, several patients with these toxicologic and psychiatric characteristics could not be safely extubated; tracheostomies were performed with protracted mechanical ventilation and patients discharged to long-term acute care hospitals. All 9 VPA-treated patients were successfully liberated from mechanical ventilation (28-170 hours after VPA) without tracheostomy.

Conclusion: VPA is a potentially effective adjunct in the management of agitation in toxicology patients. Concerns about hyperammonemia may be alleviated with levocarnitine.

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186. Takotsubo syndrome during benzodiazepine withdrawal: a case report

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Objective: Takotsubo syndrome (TTs), also known as stress cardiomyopathy is commonly associated with a transient left ventricular dysfunction sonographically referred to as "apical

ballooning". Electrocardiographic (ECG) abnormalities such as ST-segment elevation/depression, T-wave inversion, and QTc prolongation can be found with elevated cardiac biomarkers in the absence of coronary artery disease [1]. No toxicological causes of TTs have been considered in guidelines yet, although several cases have been reported in the course of acute intoxications and benzodiazepines (BDZ), alcohol and opioid withdrawal syndromes [2]. We describe a case of TTs due to BDZ withdrawal syndrome.

Case report: A 54-year-old woman was admitted to Azienda Ospedaliera-Universitaria Careggi, emergency department, after the occurrence of repeated seizures and loss of consciousness. Electroencephalography (EEG) showed no epileptic activity. She was reported to be suffering from schizoaffective disorder autonomously treated with an unknown daily dosage of alprazolam and lorazepam. No BDZs were taken during the 72 hours prior to the event. Neurological, vascular and infectious causes of her condition were diagnostically excluded. The troponin-I concentration was 1.47 µg/L and later increased to 8.17 µg/L (normal range 0.00–0.09 µg/L). Multiple ECG T-wave inversions also appeared. Cardiac sonography showed akinesia of apical areas and hyperkinesia of basal areas with an ejection fraction (EF) of 30%. A coronary catheterization was negative for artery damage, consistent with TTs. Further EEGs and magnetic resonance imaging (MRI) ruled out any organic aetiology for the status epilepticus. As the patient started recovering, withdrawal therapy with phenobarbital was promptly introduced. The patient was eventually discharged after 10 days with EF 53% and almost normalized troponin-I concentrations (0.20 µg/L), without any neurologic relapse.

Conclusion: It is likely that withdrawal syndrome plays an important role concerning TTs, because of catecholamine hyperactivity following abrupt BDZ discontinuation [3]. This case report suggests that withdrawal syndrome should be considered as a severe clinical entity owning to its risk of triggering TTs. Toxicological patients must be carefully monitored in order not to underestimate the incidence of this pathology.

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187. Food-induced methaemoglobinaemia: a case series and review

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Objective: Methaemoglobinaemia can be caused by foods containing oxidising agents. We present a case series and a review of the literature.

Methods: Western Sydney Toxicology Service covers a population of about 1.5 million. We identified 4 cases of food-related methaemoglobinaemia in our unit database over 9 years to September 2019. We also searched Pubmed and Medline using the search terms "food" and "methaemoglobinaemia." Water-related articles were excluded.

Results: In our database we found 3 patients and 4 presentations of food-related methaemoglobinaemia: a 2-year-old with a methaemoglobin level of 58% likely due to salami ingestion; a 65-year-old man with 40% methaemoglobin thought to be due to Chinese herbal tea and a 40-year-old female who presented twice with methaemoglobin concentrations of 20-25% due to a food additive labelled as "MSG". The literature search yielded 1,260 articles of which 39 were relevant. The 133 cases (including our series above) can be classified into 3 main themes:

1. Nitrate-rich vegetables: We found 29 cases in children, usually under 1 year of age, who ingested spinach, beets, chard, green beans and carrots [1]. The usually harmless nitrates are enzymatically converted by endogenous or bacterial nitrate reductases to form oxidising nitrites. This occurs with inappropriate storage or cooking, or when cooked vegetables, soups or purees are refrigerated instead of frozen. Children are especially vulnerable for several reasons: fetal Hb is easily oxidised; lower activity of reductases; lower reduced nicotinamide adenine dinucleotide (NADH) levels; and high infant gut pH, allowing more bacteria to produce nitrites.
2. Overuse of food preservatives: Nitrate- and nitrite-salts are used as anti-microbials, to redden meat, or to preserve meats such as salamis and sausages. Deliberate or accidental overuse has resulted in at least 41 cases and 1 death. Sometimes the incorrect "saltpetre" was ordered (nitrites instead of nitrates) or there was deliberate misuse in order to "freshen up" old meat, resulting in prosecutions.
3. Mistaken ingredients: There were 63 cases including 6 deaths due to adding preservatives to food instead of another ingredient. Mistaking sodium nitrite for table salt or sugar is described [2]. Occasionally nitrites are found in retail products sold as flavour enhancers.

Conclusion: Food-associated methaemoglobinaemia occurs sporadically, despite regulation, and can be fatal.

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188. Supporting the establishment of an Ethiopian Poisons Centre

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Objective: As part of an International Health Regulations [1] strengthening project, Public Health England and the UK National Poisons Information Service have been supporting St Peter's Hospital, Addis Ababa to establish the first poisons centre in Ethiopia.
Methods: An in-country needs assessment and a literature review of epidemiology of poisoning in Ethiopia have informed development of a six mission clinical toxicology staff training programme for delivery over two years. The programme combines lectures with practical workshops on effective use of poisons information databases and mentor training that includes "mock" poison enquiry calls to nurses followed by evaluation and feedback. Physicians have been identified to undertake additional distance learning in clinical toxicology adapted from a UK-based curriculum [2] and GETUP [3]. Placements at established poisons centres for Ethiopian trainees are also planned.
Results: Three training missions have been delivered including modules focused on pesticides, opioids, heavy metals, traditional medicines and operational aspects of poisons centres. Technical challenges identified whilst developing the information service related mainly to lack of reliable Internet and phone systems. These have been partially overcome by development of a database for recording enquiry data and provision of computer tablets with TOXBASE® installed that can operate offline. Capacity building challenges have involved assessing and identifying potential improvements in local toxicological laboratory services and improving the national availability of antidotes via collaboration with the Ethiopian Ministry of Health and Ethiopian Public Health Institute. The clinical treatment unit has treated over 500 patients since 2018. The poisons information centre opened in June 2019 and has started answering a small number of phone enquiries limited to local healthcare professionals during office hours.
Conclusion: Despite numerous challenges St Peter's now has a functional poison centre incorporating treatment of poisoned patients and a limited information service. Continued awareness raising, training and capacity building is essential to expand the poisons centre to a national level, develop surveillance capability and to ensure a sustainable service continues when the project concludes in 2021. The project is designed to be transferable to other countries and is also supporting an update to the 1997 WHO Guidelines for Poisons Control [4].

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189. Prevention initiatives and collaborators of the Danish Poisons Information Centre (DPIC)

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Objective: According to the WHO a poisons centre is a specialized unit providing advice on, and assistance with prevention, diagnosis and management of poisoning [1]. Suspicion of fake Xanax (alprazolam) [2] led to DPIC-collaboration with the Police and U-turn, a treatment centre for young drug users, to increase DPIC's awareness of actual illicit drug use trends among Danish youth. We aimed to measure the type and number of concerns of recreational drugs, discussed in the collaborative during the first seven months of its existence.
Methods: During the first seven months the interdisciplinary collaboration held three meetings. Moreover, three meetings were held with young former drug users. Focus was on illegal substances. We monitored the number and type of changes in the DPIC treatment guidelines during the study period, based on the concerns raised.
Results: During the meetings, information was shared about drug flow, like larger package sizes of nitrous oxide from 8 g to 580 g per unit, counterfeited pharmaceuticals like Xanax, and firsthand information about use of illegal substances. There was mutual exchange of information and in addition to gaining insight into users' experience with drugs and the healthcare system, they explained how they were often met with a low level of respect. They shared their reservations about seeking professional help. Knowledge about use of different drug distribution channels and news and trends on the illicit drug scene was also shared.
Conclusion: With increased use of potentially dangerous drugs of abuse such as cocaine and 3,4-methylenedioxymethamphetamine (MDMA) [3,4] and a growing number of counterfeit pharmaceuticals used as illegal substances, it is essential for the DPIC to focus on prevention and preparation of updated treatment guidelines. So far the collaboration has led to two changes in treatment guidelines (Xanax and nitrous oxide). It is therefore expected that the collaboration consisting of the police, U-turn, the DPIC and input from former users, will continue to increase insight and changes in the way we treat poisoned patients. Information gathered from the interdisciplinary collaboration is unique as published data are sparse.

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190. Risk assessment and lessons learned: a collaboration between Public Health and a National Poisons Information Centre

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Objective: The National Poisons Information Centre (NPIC) provides advice to healthcare professionals and the public in managing potential poisonings in Ireland. Departments of Public Health (DPH) have a legal responsibility to investigate threats that have the potential to harm the public. To strengthen relationships between these two agencies, we undertook a retrospective risk-assessment of public health incidents reported to NPIC from a public health perspective, to describe the incidents and suggest a public health response.
Methods: We defined a public health incident as an incident that involved three or more members of the public. We retrospectively, risk-assessed public health incidents reported to NPIC between 1 January 2015 and 31 December 2016, from a public health perspective, using the US Environmental Protection Agency five step Human Health Risk Assessment [1].
Results: Forty-nine enquiries to NPIC, relating to 36 unique and varied incidents met the case definition. Most incidents (55.6%) were reported by members of the public and chemical incidents (27.8%) were most commonly reported. A public health risk-assessment was carried out in 15 of the incidents (Table 1). The incidents included chemical spills, contamination of recreational and drinking water and carbon monoxide exposure. Following risk-assessment of incidents, potential public health interventions could include: decontamination and exposure minimisation advice, water-supply monitoring and "do not use" advice, liaison with local authorities regarding signage and safety recommendations, advice on carbon monoxide remediation measures and household safety messages for the public.
Conclusion: A variety of public health incidents are reported to NPIC. A systematic approach using the Human Health Risk Assessment tool is useful for DPH to risk-assess the situation. Ongoing collaboration between NPIC and DPH will facilitate public health surveillance, identification of remediation measures, sharing of expertise and knowledge and training opportunities.

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191. Myocardial infarction in the acutely poisoned patient: a case series

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Objective: Myocardial infarction (MI) is a cardiology emergency. Although coronary occlusion by an atheromatous plaque is usually the first cause of MI, environmental, accidental or voluntary poisoning may represent alternative etiologies. Our objective was to determine the prevalence and identify the involved toxicants in MI onset in the acutely poisoned patient.
Methods: We conducted a retrospective single-centre cohort study including all poisoned patients admitted to the intensive care unit (ICU) in 2007-2019 who developed MI (evidenced by repeated electrocardiograms, elevation in cardiac biomarkers and/or compatible coronary angiogram), with a compatible chronology supporting the causality of the toxic exposure or its direct consequences in the onset of the myocardial infarction.
Results: Fourteen patients (11 males/3 females, median age of 59 years) among the 5400 poisoned patients admitted in the 12 year period (prevalence of 0.26%) presented a MI. The main toxic etiologies of MI were cocaine (36%, resulting in the rapid patient death in relation to this complication in 4/5 patients), beta-blockers (22%) and metformin (14%). Carbon monoxide, usually cited in the literature as possible cause of chemical-induced MI, was only responsible for one case (7%). The patients developed

Table 1. Number of public health incidents reported to National Poisons Information Centre (NPIC), Ireland, 2015-2016, by poison category, source of call, location of incident and exposure route.

Details of incident	Number of incidents	%	Public health risk assessment required (n)
Category of poison			
Chemical	10	27.8	5
Fuel	6	16.7	4
Gas	6	16.7	0
Plastic	4	11.1	1
Other (paint, rat poison, food hazard, chlorine, lead, insulation foam)	10	27.8	5
Source of call			
Member of the public	20	55.6	–
GP	12	33.3	–
Hospital	4	11.1	–
Other (ambulance, community pharmacist, public health doctor, other)	4	11.1	–
Incident location			
Private house	28	77.8	–
Work/school	4	11.1	–
Other (public place, other)	4	11.1	–
Exposure route			
Inhalation only	21	58.3	–
Ingestion only	12	33.3	–
Inhalation and ingestion	1	2.8	–
Inhalation, ingestion and skin contact	1	2.8	–

cardiovascular failure with ST segment elevation on the electrocardiogram (ECG) leading to cardiac arrest (57%) or conduction impairment with modifications of the QRS complex morphology (50%). The remarkable elevation in troponin (median value of 36 µg/L on admission peaking at 5,413 µg/L) and brain natriuretic peptide (BNP, median value of 148 pg/mL on admission peaking at 592 pg/mL) clearly supported the clinical severity of these presentation. Supportive treatments included fluids (100%), mechanical ventilation (93%), catecholamine infusion (86%), renal replacement therapy (57%) and veno-arterial extracorporeal membrane oxygenation (VA ECMO) (43%). Platelet antiaggregant drugs including salicylates (86%) were systematically administered. Death rate was 57%.
Conclusion: MI may be related to acute poisoning by a direct drug-induced mechanism or an indirect mechanism related to the initial complications. MI onset in this condition is associated with a very poor prognosis.

192. Diphtheria: two cases treated with antitoxin

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Objective: Diphtheria (*Corynebacterium diphtheriae*) is a rare disease in developed countries, but fatality rates worldwide are high. Gold standard treatment is early administration of diphtheria antitoxin (DAT equine serum) in association with antibiotic therapy. DAT should be administered as soon as clinical suspicion is made, before laboratory confirmation [1]. Although DAT is listed in the WHO Essential Medicines for Children, it is often unavailable. Sporadic cases of diphtheria have been reported recently in Europe, and in one of these, the delay in DAT availability resulted in death [2]. We describe two cases of use of DAT from the Pavia Poison Control Centre (PPCC) stockpile.
Case series: In Italy, DAT has been available from the PPCC since November 2016 (30 vials 10 mL/10,000 IU; Indian product). The PPCC managed 2 patients with suspected diphtheria between November 2016 and September 2019. Case 1. A 79-year-old woman was admitted to the emergency department (ED) with fever, pharyngodynia, swelling of the neck, and pseudomembranes on the pharynx; diphtheria was suspected and a complete dose of 10 vials was administered to the patient. Laboratory tests resulted negative. Case 2: A 65-year-old man was admitted to the ED with dysphonia, fever, dyspnea, and pseudomembranes on the bronchial tree; diphtheria was suspected and a complete dose of 10 vials was administered to the patient. Laboratory diagnosis confirmed the case as caused by the potentially toxin-producing *Corynebacterium ulcerans*. Neither patient developed any adverse effects from DAT administration.
Conclusion: In most industrialised countries diphtheria has been eradicated following mass vaccination campaigns, but migration from countries where diphtheria is still endemic and/or countries with lower vaccination coverage may pose a risk for the return of the disease. Despite the laboratory tests, DAT availability in Italy allowed correct management of suspected diphtheria cases. As diphtheria outcome depends on how early antitoxin treatment is started, it would be useful to establish a DAT stockpile network within EU Member States, in order to ensure that antitoxin therapy can be supplied in a timely manner throughout Europe. Poison Centres should consider the possibility of including DAT in their stockpiles. Moreover, institutions responsible for regulatory activity should simplify procedures for import of DAT from non-EU countries.

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193. QTc interval and electrolyte derangement in alcohol withdrawal-related seizures

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Objective: Seizures are common in severe alcohol withdrawal syndrome (AWS). During AWS, QTc prolongation and electrolyte derangement may occur which themselves can predispose to seizures. Our objective was to determine the relationship of QTc, hypomagnesaemia and hypokalaemia to seizures in patients with AWS.
Methods: A retrospective review of patients admitted to the medical wards of a central London acute NHS Trust (January-December 2018) with AWS and AUDIT-C score ≥20 was conducted. Data collected included demographics, hospital admission 12-lead ECG, QTc (ms) measured by 12-lead ECG, serum potassium and magnesium concentration.
Results: Overall, 86 patients presented with AWS seizures over the 12 month study period; 75 were male (87%), mean age 47 ± 10.19 years) (range 26-67). Self-reported alcohol intake ranged from 30-580 units/week (mean 185 ± 130 units/week). Seizures occurred out-of-hospital in 63 cases (73%); 6 seizures (7%) occurred out-of-hospital and in the Emergency Department (ED), 12 (14%) occurred from admission to hospital, and for 5 seizures (6%) the location was not documented. In the study group 25 patients (29%) had no previous seizure history. QTc interval: Most patients (62, 72%) had a 12-lead ECG at hospital admission. QTc was documented in 52 patients, with a mean QTc of 444 ± 20 ms (range 405-485 ms). Seventeen patients (20%) had a prolonged QTc, 15 (17%) were men with a QTc >440 ms, with 2 women having a QTc >470ms. Electrolytes: Magnesium concentrations were checked in 51 patients (59%) (mean 0.76 ± 0.17 mmol/L) and potassium concentrations checked in 82 patients (95%) (mean 3.98 ± 0.59 mmol/L). Eleven (13%) had hypomagnesaemia (<0.65 mmol/L) ranging between 0.3-0.64 mmol/L. Fifteen (17%) had hypokalaemia (<3.5 mmol/L) ranging between 2.53-3.4 mmol/L. Eight (9%) had both hypomagnesaemia and hypokalaemia. Alcohol consumption (units/week) was not significantly correlated to serum magnesium (Pearson's correlation coefficient $r = 0.02$, $p = 0.89$) or potassium concentrations ($r = 0.12$, $p = 0.34$). QTc duration was inversely correlated to serum magnesium ($r = -0.37$, $p = 0.053$) and potassium concentration ($r = -0.36$, $p = 0.01$).
Conclusion: Hypomagnaesmia, hypokalaemia and prolonged QTc were common findings in patients with AWS seizures. However, a significant proportion of patients did not have these checked suggesting that the potential for derangement may not be

recognised as part of standard management. Potassium concentration was significantly inversely correlated to QTc in patients with seizures, while magnesium concentrations trended toward significance. Electrolyte derangement may predispose to prolonged QTc in patients with AWS seizures in addition to increased adrenergic activity that is observed. Physiologically these changes may be predictive of seizure activity, however additional studies are needed to evaluate this further.

194. A significant troponin rise in a patient following accidental ingestion of pimobendan

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Objective: To report a case of accidental human ingestion of veterinary pimobendan presenting to an Australian Emergency Department (ED).
Case report: A 68-year-old female presented to ED on the advice of the New South Wales Poisons Information Centre (NSWPIC) 2 hours after inadvertently ingesting 2.5 mg of her dog's pimobendan. She had a history of well controlled hypertension. Her examination and vitals were unremarkable on admission. Her initial ECG showed normal sinus rhythm with a rate of 65, normal QRS complexes, QTc and PR intervals, with nil ST segment or T wave changes. Her pathology showed acutely elevated cardiac troponin I (CTnI) of 1296 ng/L at 2 hours post-ingestion. The serial CTnIs at 4 and 10 hours post-ingestion were 4138 ng/L and 3174 ng/L, respectively. Repeat vitals and ECGs at these time points were unremarkable and the patient remained asymptomatic. Her chest X-ray was normal. She was medically treated as per protocol for a non-ST-elevation myocardial infarction (NSTEMI). Her subsequent coronary angiogram demonstrated minor disease. The recovery ECG showed new T wave inversion in lateral leads (I, aVL) and subsequent echocardiogram showed normal left ventricular size and function. The patient was discharged 1 day post-admission without reduction in functional outcome.
Conclusion: Documented cases of human pimobendan toxicity are rare despite being the most commonly ingested veterinary agent reported to NSWPIC [1]. Here, we present a case of acute troponin rise post-ingestion of a single dose of pimobendan in an otherwise healthy individual. Though a dose of 2.5 mg was not enough to elicit a significant hemodynamic compromise, it is likely that it may have significantly increased cardiac metabolic demand leading to hypoxia and subsequent ischemia resulting in a type 2 myocardial infarction-like event. The patient's existing coronary artery disease likely also contributed to myocardial hypoperfusion. Taken together with findings from emerging cases suggesting strong potential for harm with accidental low to moderate dose ingestions, we recommend patients present for medical assessment regardless of dosage of exposure.

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195. Antidote treatment in viper envenomation in Italy: a comparison of 4 antivenoms during a 6 year study

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Objective: Different antivenoms are available in Italian hospitals. Clinical response to treatment with different antivenoms was prospectively evaluated in patients presenting with Grading Severity Score (GSS) ≥ 2 during a 6 year study period.
Methods: Data on all consecutive viper-bitten patients referred to our Poison Control Centre (PCC) from 2013-2019 were collected for sex, age, site of bite, time between bite and Emergency department (ED) admission/antivenom administration (intravenous), antivenom and number of vials, GSS and clinical response (improvement/worsening after 6 hours), need of adjunctive doses, and adverse effects. Clinical manifestations were evaluated according to the GSS. Continuous variables' distribution was expressed with median and interquartile range. Univariate and multivariate mixed effects logistic regression was applied to estimate the probability of improvement based on the variables measured.
Results: Overall 114 patients (51 years (35-67); male 72.8%) were included; 19 were pediatric (1-16 years). *Vipera aspis* was mainly involved. Upper and lower limbs were involved in 83% and 17% of cases, respectively. Time between bite and ED admission was 2 hours (1-4) and showed: GSS-0 in 2/114 (1.75%), GSS-1 in 57 (50%), GSS-2 in 45 (39%) and GSS-3 in 10 patients (9%). Time between bite and antivenom administration was 10 hours [5-20] in GSS-2 and GSS-3 patients, respectively. The 4 available antidotes were administered with a different frequency: Viper Venom Antitoxin® in 61/114 cases (54%), European Viper Venom Antiserum® in 31 (26%), and both ViperaTab® and Viekvin® in 11 cases each (10%). For all antiserum, a first dose of 1 or 2 vials was administered in 43 and 74/114 cases, respectively. A clinical improvement was registered after 6 hours in 79/117 patients (69%). Seventeen patients needed a second dose (1 vial) of antivenom: 10/17 Viper Venom Antitoxin®, 4/17 European Viper Venom Antiserum®, 2/17 ViperaTab®, and 1/17 Viekvin®. Nine (9/17; 53%) re-treated patients received Viper Venom Antitoxin® as first dose. Multivariate analysis identified the following as factors increasing the probability of improvement: the use of European Viper Venom Antiserum® and Viekvin® (p 0.001 and 0.041, respectively) compared to Viper Venom Antitoxin® (baseline). The mean length of hospitalization was 5 days [4-7]. Acute adverse reactions were registered in 3 patients (2 mild-hypotension, 1 urticaria; all 3 treated with European Viper Venom Antiserum®) and mild serum sickness in 1 patient (treated with Viper Venom Antitoxin®). No lethal cases were registered.
Conclusion: Our experience found that European Viper Venom Antiserum® and Viekvin® are more effective in counteracting the venom toxicity of Italian vipers than ViperaTab® or Viper Venom Antitoxin®. In general, the 2 vial regimen as first dose offers better probability of clinical improvement, in adults and children.

196. Is fentanyl responsible for more severe neuro-respiratory depression than morphine? A rat *in vivo* investigation

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Objective: The opioid overdose crisis that has resulted in thousands of deaths up to date is a major public health issue, not only in the US but also in Europe. In the US fentanyl and its analogues have become the main cause of opioid overdose-related fatalities. These molecules are potent mu-opioid receptor agonists, up to 10,000 times more potent than morphine, the reference opioid. We aimed to characterize the neuro-respiratory response of fentanyl in comparison to morphine.
Methods: The neuro-respiratory effects of intravenous morphine and fentanyl at 50% of their respective LD_{50} were investigated in comparison to saline in the rat using a clinical sedation scale, the body temperature measurement, plethysmography, diaphragmatic electromyography (EMG), arterial blood gas and blood lactate measurements. The measurement of the serum concentrations of morphine, fentanyl and their respective metabolites was performed using liquid chromatography coupled to mass spectrometry in tandem. The pharmacokinetics and pharmacokinetic/pharmacodynamic relationships were modeled and compared between both opioids.
Results: Morphine-induced respiratory depression manifested by a significant increase in the inspiratory time and decrease in the minute volume, as generally characterizing opioids, in combination with significant hypoxemia and respiratory acidosis. Fentanyl significantly induced more marked respiratory depression than morphine, accompanied by an increase in the expiratory time and tidal volume ($p < 0.01$), a decrease in serum bicarbonate ($p < 0.05$) and increase in blood lactate ($p < 0.05$). No significant differences between morphine and fentanyl were observed regarding their effects on rat body temperature and sedation. The EMG showed a short-term increase in the amplitude of diaphragmatic contractions with morphine but not with fentanyl. The pharmacokinetic/pharmacodynamic relationship modeling allowed understanding of the differences between the effects of both opioids.
Conclusion: The neuro-respiratory toxicity of fentanyl is more marked than that with morphine with the absence of a fentanyl-induced diaphragmatic compensation mechanism of central respiratory depression.

197. Analytically-confirmed exposure to new psychoactive substances in patients with severe clinical toxicity in the UK, 2015-2018: a report from the IONA study

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Objective: The Identification Of Novel psychoActive substances (IONA) study analyses clinical samples from UK emergency department attendees with suspected severe toxicity caused by new psychoactive substances (NPS). Here we describe trends in NPS identified between March 2015 and December 2018.
Methods: Patients (≥16 years) presenting to participating hospitals with severe acute toxicity (pre-defined definitions) after suspected NPS exposure were included after informed consent (or agreement of a relative/representative if lacking capacity). Demographic and clinical features were recorded using a structured data collection sheet. Blood and/or urine samples were analysed by liquid chromatography-tandem mass spectrometry.
Results: Analytical and clinical data were available for 471

Table 1. Annual numbers (proportions, %) of patients with at least one sample positive for NPS, 2015 to 2018 in the IONA study. Selected NPS groups/substances with at least 20 exposed patients. The 5 most common traditional drugs of misuse are also shown for comparison.

	2015	2016	2017	2018	Overall
Patients recruited (n)	56	173	164	78	471
Hospitals recruiting (n)	4	12	20	22	25
Patients with sample positive for					
Any NPS	41 (73%)	117 (68%)	74 (45%)	38 (49%)	272 (58%)
Synthetic cannabinoid receptor agonists (SCRA)	24 (43%)	77 (45%)	45 (27%)	31 (40%)	177 (38%)
Cathinones	4 (7.1%)	19 (11%)	10 (6.1%)	6 (7.7%)	39 (8.3%)
NBOMe compounds	5 (8.9%)	6 (3.5%)	10 (6.1%)	0 (0%)	21 (4.5%)
Individual NPS					
5F-ADB	0 (0%)	43 (24.9%)	26 (15.9%)	9 (11.5%)	78 (16.6%)
FUB-AMB	3 (5.4%)	21 (12.1%)	28 (17.1%)	6 (7.7%)	58 (12.3%)
MDMB-CHMICA	16 (28.6%)	21 (12.1%)	12 (7.3%)	6 (7.7%)	55 (11.7%)
5F-NPB-22	1 (1.8%)	22 (13%)	3 (1.8%)	1 (1.3%)	27 (5.7%)
5F-PB-22	3 (5.4%)	21 (12.1%)	0 (0%)	2 (2.6%)	26 (5.5%)
Methiopropamine	5 (8.9%)	4 (2.3%)	0 (0%)	0 (0%)	21 (4.5%)
Traditional drugs of misuse					
Any	44 (79%)	141 (82%)	146 (89%)	65 (83%)	399 (85%)
Diazepam	20 (35.7%)	59 (34.1%)	60 (36.6%)	25 (32.1%)	164 (34.8%)
Methadone	15 (26.8)	67 (38.7)	45 (27.4)	11 (14.1)	138 (29.3)
Cocaine	15 (26.8)	31 (17.9)	68 (41.5)	21 (26.9)	135 (28.7)
3,4-methylenedioxymethamphetamine (MDMA)	6 (10.7%)	21 (12.1%)	37 (22.6%)	21 (26.9%)	85 (18.0%)
Methamphetamine	14 (25.0%)	26 (15.0%)	14 (8.5%)	6 (10.3%)	62 (13.2%)

patients (median age 30 years, range 16-72) including 378 (80%) males. NPS were identified in at least one sample from 272 (58%) patients, traditional drugs of misuse in 399 (85%), both in 213 (45%) and no drug of misuse in 17 (3.6%). In spite of increasing numbers of recruiting hospitals, the annual numbers of patients recruited with suspected severe NPS toxicity fell after 2016. Comparing data collected after 1 January 2017 with that collected before, the proportions with samples positive for NPS overall ($P < 0.001$), synthetic cannabinoid receptor agonists (SCRA, $P < 0.005$) and specifically MDMB-CHMICA ($P < 0.005$), 5F-NPB 22 ($P < 0.001$) and 5F-PB 22 ($P < 0.001$), as well as methamphetamine ($P < 0.01$) have fallen. The proportion positive for cocaine (or metabolites) increased in 2017, but this was not maintained in 2018.

Conclusion: Recruitment of patients with suspected severe NPS toxicity has become increasingly difficult and those recruited have analytically-confirmed NPS exposure less often. This probably reflects reduced NPS use following generic control of psychoactive substances (May 2016) and increased law enforcement and trading standards action. The possibility that some previous NPS users may switch to traditional drugs (e.g. cocaine) needs careful monitoring.

198. Increasing abuse and addiction to nitrous oxide (N_2O): still a legal high in Denmark

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Objective: Insufflation of 100% N_2O from whipped cream cartridges has gained increased interest as a recreational drug among the younger population aged 15-35 years of age. N_2O cartridges are available in boxes of 10-100 in kiosks and Internet shops. The gas is emptied into a balloon using a designed device and inhaled directly from the balloon. Acute effects include impaired physiological response to hypoxia if the inhaled concentration exceeds 50% and dizziness and confusion progressing to asphyxia. Chronic effects from prolonged recreational use cause "inactivation" of vitamin B12 and irreversible blockade of methionine synthase. At present, a safe dose threshold has not been established. We aimed to evaluate the trends in abuse of N_2O, and the correlation between acute intoxication and abuse and chronic intoxications with neurologic deficit.

Methods: Calls to the DPIC 2013-2019 from the public and healthcare institutions regarding acute and chronic exposure/abuse to 100% N_2O were recorded. Upon initial contact to the DPIC, acute exposures were divided into categories according to the symptoms present; None, Mild/moderate (lethargy) or Severe (sedation/coma), and chronic exposures into categories None, Mild/moderate (paresthesia of extremities) or Severe (anemia/organ dysfunction/cognitive dysfunction). Chronic abuse was defined as >50 cartridges/day exceeding 5 days.

Results: Calls regarding N_2O first occurred in 2013 (Table 1), and since 2015 the number of calls and the severity of poisoning has increased steadily. All chronic exposure group patients, except for two patients, experienced neurologic deficits and symptoms included peripheral neuropathy, tetraplegia, ataxia and/or cognitive dysfunction. Data showed a relationship between dose and severity of symptoms, but a few chronic cases recently reported severe symptoms from daily doses of less than 50 cartridges.

Conclusion: Based on data a safe dose of N_2O might be lower than 50 cartridges/day for 5 continuous days. Long-term effects from acute or prolonged use are not yet established.

199. Risk factors for esophageal stricture in alkali ingestion in children

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Table 1. Number (n) of patients registered to the Danish Poisons Information Center (DPIC) with acute or chronic nitrous oxide use, 2013-2019 (9 months).

	Acute exposure					Chronic exposure				
Year (total)	N	Dose, number of cartridges (n)	Symptoms None, n	Mild/moderate (lethargy), n	Severe (sedation/coma), n	N	Dose, number of cartridges (n)	Symptoms None, n	Mild/moderate (Paresthesia of extremities), n	Severe (anemia/organ dysfuncition/cognitive dysfunction), n
2013 (1)	1	NR (1)	1	–	–	0	–	–	–	–
2014 (2)	2	<50 (1), >50 (1)	0	0	2	0	–	–	–	–
2015 (8)	7	<50 (7)	4	2	1	1	>50 (1)	0	1	0
2016 (13)	11	<50 (3), >50 (1), NR (7)	4	6	1	2	NR (2)	0	0	2
2017 (12)	8	<50 (1), >50 (2), NR (5)	2	4	2	4	<50 (1), >50 (0), NR (3)	1	2	1
2018 (31)	25	<50 (7), >50 (8), NR (10)	7	11	7	6	<50 (1), >50 (5), NR (0)	0	1	5
2019/9 mths (39)	19	<50 (13), >50 (3), NR (3)	9	4	6	20	<50 (3), >50 (10), NR (7)	3	6	11

NR: not reported.

Objective: To assess the risk factors for esophageal stricture a late complication of alkali ingestion in children.
Methods: A retrospective analysis of medical records of all patients admitted after strong alkali ingestion to a pediatric poisoning center, over a four year period. Data collected were: clinical features during the acute period and esophageal findings revealed by the upper digestive endoscopy. Statistical testing was performed using the chi-squared test or Mann-Whitney U Test, and P-values lower than 0.05 were considered as statistically significant.
Results: A total of 72 children aged 1-18 years with strong alkali ingestion were admitted in our center between April 2015 and August 2019. According to the di Constanzo classification [1] the following findings were revealed by the initial endoscopy performed in the first 72 hours: zero degree injury in 24 patients (66%), first degree in 18 (25%), second degree in 22 (30%), and third degree in 8 (11%). The second endoscopy was performed between day 21 and day 28 after ingestion and detected esophageal stricture in 8 patients (11%). All the 8 patients presented severe symptomatology during the acute period (vomiting, gastrointestinal bleeding or acute respiratory failure), but only gastrointestinal bleeding could be statistically correlated with the presence of esophageal stricture ($p = 0.04$). There was a statistical correlation between the degree of initial esophageal injury and the development of the esophageal stricture ($p = 0.011$) [2] as follows: 5 cases with third degree lesions, 1 with second degree lesions and 2 with first degree lesions. The therapeutic approach in patients with caustic esophageal stricture included repeated esophageal dilatation in 5 children and gastrostomy pending esophagoplasty in 2 cases. One patient did not return for the scheduled follow-up.
Conclusion: In this study the presence of esophageal stricture could be correlated with the severity of the initial esophageal lesion [2], and most cases involved had second and third degree lesions. Gastrointestinal bleeding during the acute phase represents a risk factor for the development of the esophageal stricture, but further studies are necessary to confirm this hypothesis as the main limitation of the study was the rather small number of cases.

References

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[2] Calello DP, Henretig FM. Acids and alkalis. Pediatric toxicology diagnosis and management of the poisoned child. The McGraw-Hill Companies Inc.; 2005.

200. Efficacy of a 12h intravenous acetylcysteine (SNAP) regimen following single acute paracetamol overdose

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Objective: To compare the efficacy of a modified 2-bag 12h acetylcysteine (NAC) regimen ('SNAP') which causes fewer adverse reactions to the currently licensed 3-bag 21h NAC regimen used to treat paracetamol poisoning [1].
Methods: The modified 12h "SNAP" regimen (intravenous NAC 100 mg/kg over 2h then 200 mg/kg over 10 h), was introduced in 2016 in two UK hospitals to treat all patients requiring NAC for paracetamol overdose. Data was collected prospectively for 3 years after "SNAP" introduction in each hospital and compared to data from previous audits of patients treated with the conventional 21h regimen. We determined the proportion of patients who developed a peak ALT >1000 with each regimen. We performed a logistic regression analysis to determine the odds of developing a peak ALT >1000 or peak INR >2 with each regimen before and after adjustment for covariates (time to treatment, nomogram band, dose ingested and admission ALT).
Results: The proportion of patients who developed peak ALT >1000 with the SNAP and conventional regimen were not significantly different in each risk category (Table 1). The risk of developing a peak ALT >1000 was not significantly different between patients treated with the 12h regimen and the conventional 21h regimen before (crude OR 0.810, 95% CI 0.39-1.68, $p = 0.572$) or after adjustment for covariates (adjusted OR 0.692, 95% CI 0.32-1.51, $p = 0.354$). The risk of developing a peak INR >2 was not significantly different between the two groups (crude OR 1.24, 95% CI 0.49-3.13, $p = 0.65$) or after adjustment for covariates (adjusted OR 1.04, 95% CI 0.39-2.72, $p = 0.94$).
Conclusion: A simpler 12h acetylcysteine regimen appears to be comparable in efficacy to the conventional 21h regimen in all risk groups, but requires confirmation in larger cohorts of patients before routine implementation into clinical practice.

Reference

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Table 1. Proportion of patients developing peak ALT >1000 IU/L in those treated with the conventional 21 hour N-acetylcysteine regimen and the 12 hour (SNAP) regimen.

	Conventional 21 hour regimen (n = 338)			SNAP 12 hour regimen (n =854)		
Time to N-acetylcysteine treatment	Nomogram band	Nomogram band	Total	Nomogram band	Nomogram band	Total
≤8 hours	0/107	4/90	4/197	0/294	7/230	7/524
	(0%)	(4.4%)	(2.0%)	(0%)	(3.0%)	(1.3%)
>8 hours	1/64	6/77	7/141	2/155	12/175	14/330
	(1.6%)	(7.8%)	(5.0%)	(1.3%)	(6.9%)	(4.2%)
Total	1/171	10/167	11/338	2/449	19/405	21/854
	(0.6%)	(6.0%)	(3.3%)	(0.5%)	(4.7%)	(2.5%)

201. Comparison of the Australian and New Zealand Referral Criteria versus the King's College Criteria to predict mortality or liver transplant in paracetamol overdose

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Objective: Paracetamol overdose is common and can lead to fulminant hepatic failure. In cases that are not improving with standard medical therapy with N-acetylcysteine, some patients may require liver transplant. The King's College Criteria (KCC) is the most widely used survival predicting model, however, it is limited by its low sensitivity. The Australia and New Zealand (ANZ) referral criteria incorporates several additional markers but has not been extensively studied for its predictive value. The focus of this study was to compare the ANZ referral criteria versus the KCC for predicting mortality and morbidity in paracetamol overdose.
Methods: This study involves a retrospective analysis of patients presenting to the Austin Hospital between 2010 and 2019 with paracetamol overdose requiring treatment with N-acetylcysteine. We evaluated 983 paracetamol overdose cases from 2010 to March 2019. The primary outcome was death or transplant. Sensitivity and specificity, along with associated receiver operating characteristic (ROC) curves were determined for both models to predict the primary outcome. Binary logistic regression was performed on both the KCC and ANZ referral criteria, subsequent backward stepwise elimination was applied.
Results: A total of 481 cases were identified who met the inclusion criteria; 18 cases (3.7%) met the composite endpoint of death or transplant. The ANZ referral criteria has a higher sensitivity (100%, 95% CI 81.5,100), but lower specificity (88.3%, 95% CI 85,91.1) than the KCC. The ROC-area under the curve (AUC) for the KCC was 0.868 (95% CI: 0.760, 0.977), the ROC AUC for the ANZ referral criteria was 0.627 (95% CI: 0.547, 0.707). Cohen's Kappa was calculated to be 0.449, showing moderate agreement between the KCC and ANZ referral criteria. On logistic regression, after backward stepwise elimination, the final regression model for the KCC included 3 variables: serum creatinine >300 mmol/L, persistent acidosis with a pH <7.3 and high-grade encephalopathy. The final model for ANZ criteria included serum creatinine >200 mmol/L, persistent acidosis with pH <7.3 and systolic hypotension.
Conclusion: The ANZ referral criteria compared to the KCC was more sensitive for the outcome of mortality and transplant in paracetamol overdose. This is important for screening patients that may become unstable and difficult to transfer at a later stage of their admission. Further development on the ANZ referral criteria should consider a combination of the 3 variables: persistent acidosis, systolic hypotension and serum creatinine as higher risk predictors.

202. Three years of experience implementing a chemical submission protocol at an Emergency Department

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Objective: Chemical submission (CS) is the surreptitious administration of psychoactive substances with criminal intent. In 2016 a multidisciplinary ED-protocol was created to homogenise and systematise care of patients with suspected CS, sometimes related to drug-facilitated sexual assault (DFSA). We analyse clinical and toxicological characteristics of cases in which the CS protocol was activated during the first two years of implementation.
Methods: Patients presenting to the Emergency Department (ED) with suspected CS from 1 May 2016 to 3 September 2019 were included. Age, sex, residence, substances admitted to have been taken, CS location, arrival to ED, toxins detected (ethanol in serum, cannabis, cocaine, benzodiazepines, opiates, amphetamines and ecstasy in urine by immunoassay, gamma-hydroxybutyrate (GHB), scopolamine, ketamine, general drug screening and confirmation of positive immunoassays in urine by gas chromatography-mass spectrometry (GC-MS)) and initial clinical situation were analysed. DFSA was also analysed, using the same variables.
Results: Overall 191 patients were treated, 0.03% of the ED presentations over the same period, 149 women (78%), with mean age 26.4 years. Most victims were local residents (n = 98, 51.3%) and 45 (23.6%) arrived by ambulance. In 133 cases (69.6%), ethanol was present, most events occurred in a bar (68, 35.6%) or nightclub (27, 14.1%). The most frequent symptoms were amnesia (78.5%) and confusion (50.3%). After alcohol (73.8%), the most common toxins were cocaine (n = 36, 18.8%) and cannabis (n = 33, 17.3%). CS in patients with DFSA (n = 94, 49.2%) compared to CS not involving DFSA (n = 97, 50.8%), differed in mean age, gender (female, $p < 0.001$), and in symptoms (confusion, anxiety and in decrease in consciousness) ($p < 0.05$).
Conclusion: A CS protocol standardises the response to these presentations. Ethanol was the most common toxin, followed by

Table 1. The characteristics of victims presenting with suspected chemical submission with and without drug-facilitated sexual assault (DSFA).

Variable	DFSA (N, %)	No DFSA (N, %)	p value (chi-squared)
N	94 (49.2%)	97 (50.8%)	
Age (mean)	24.7%	29.3%	0.0001
Location of incident			0.0791
Local resident	42 (44.7%)	56 (67.7%)	
Foreigner	52 (55.3%)	41 (42.3%)	
Place			
Bar	28 (29.8%)	41 (42.3%)	0.1001
Discotheque	30 (31.9%)	30 (30.9%)	0.8832
Home	19 (20.2%)	17 (17.5%)	0.7721
Public road	17 (18.1%)	9 (9.3%)	0.1180
Symptoms			
Amnesia	75 (79.8%)	75 (77.3%)	0.8811
Confusion	56 (59.8%)	40 (41.2%)	0.0169
Anxiety	11 (11.7%)	31 (31.3%)	0.0014
Decrease in consciousness	13 (13.8%)	30 (30.9%)	0.0079
Laboratory confirmed drugs			
Cannabis	18 (19.1%)	16 (16.5%)	0.7717
Cocaine	20 (21.3%)	16 (16.5%)	0.5094
Benzodiazepines	10 (10.6%)	9 (9.3%)	0.9425
Amphetamine	5 (5.3%)	8 (8.3%)	0.6059
GHB	1 (1.1%)	3 (3.1%)	0.6358
Ketamine	1 (1.1%)	2 (2.1%)	0.5792
Scopolamine	1 (1.1%)	0	0.9874
Average stay (hours)	5:17	5:28	
Arrived by ambulance	17 (18.1%)	28 (28.9%)	0.1130
Gender woman	89 (94.7%)	60 (61.9%)	0.0001
Alcohol previous use	69 (73.4%)	64 (65.9%)	0.3379

cocaine and cannabis. DFSA-CS cases were younger, more likely female, and non-residents, with amnesia and confusion predominant symptoms.

203. Emergent toxicological molecular screening test on ICU admission: can it be trusted?

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Objective: Acute poisonings represent a frequent cause of intensive care unit (ICU) admission. Establishing a rapid reliable analytical analysis on ICU admission is essential to avoid clinical misdiagnoses and optimize management. We set up a screening molecular testing named "Emergent Toxicological Screening" (ETS) based on the combination of ultra-performance high-pressure liquid chromatography coupled to ultraviolet spectrophotometry + mass spectrometry to screen all ICU poisoned patients. The results of the ETS could be available in 3 hours. We designed this study to evaluate the clinical usefulness and diagnostic limitations of our ETS.
Methods: We conducted a single-centre observational cohort study including all poisoned patients admitted to the ICU over one year. We retrospectively collected information on the presumed ingested toxicants with the ingested doses, the patients' long-term treatments and the results obtained from the admission samples using ETS, enzymatic and colorimetric screening tests as well as the results of the reference assays of our laboratory. We determined the reasons and rates of discordance between the toxicants presumably ingested, identified using the ETS and the reference assays.
Results: Overall 451 poisoned patients (55% males/45% females; age 41 years [28–56] (median [25th-75th percentiles])) were included. The most common toxicants were psychotropic drugs (30%), illicit drugs (16%) and cardiotoxicants (12%). The main reasons for discordance with ETS were the non-reliability of medical history due to patient consciousness impairment/confusion (37%), the known technical limitations of ETS (34%) and the identification of drugs administered in the pre-hospital setting or emergency department (17%). A unexpected lack of sensitivity was observed in 7% of the cases in comparison to the analytical methods of reference. The only false positive result was the detection of quinine in relation to the consumption of energy drinks by patients in the days prior to admission.
Conclusion: With limited unexpected false negative results (7%) and just a single situation of false positive, ETS appears reliable, specific and sufficiently sensitive especially to screen for psychotropic and cardiotropic pharmaceuticals usually involved in poisonings in developed countries. In combination with the usual enzymatic and colorimetric screening tests, ETS offers an extensive coverage of toxicants, but all ETS-identified molecules remain to be confirmed by specific assays in the days following ICU admission for a definitive diagnosis.

204. Bedside formate analysis in methanol poisoned patients: a pilot study

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Objective: Diagnosis of methanol poisoning and evaluation of a metabolic acidosis in the severely ill patient can pose a major challenge. Even in areas where specific analyses are routinely performed there is often a delay from sampling to results, and in rural areas these analyses frequently do not exist at all. A semi-quantitative test strip provides a rapid (3-4 minutes) identification of samples that can be performed bedside. Three different ranges on the strips allow immediate start of treatment in all patients with formate concentrations where symptoms/signs from methanol poisoning can be expected (>10 mmol/L). All low-positive results are recommended to be followed by a second sample within 2-4 hours. If still low or negative, no symptoms can be expected and specific treatment with antidote etc. can be postponed or omitted. We tested a prototype of a formate point-of-care test on a patient where the gold standard gas chromatographic mass spectrophotometry (GC-MS) initially gave a false positive methanol concentration (0.3 g/L; 9.4 mmol/L) in a patient presenting with a severe metabolic acidosis of unknown origin. A set of two different serum samples spiked with formate and a negative control was also added to this pilot study.
Methods: The admission serum sample was analyzed by GC-MS for measuring methanol and formate (with good linearity within 0.2-1.0 g/L [6-31 mmol/L] and 0.25-20 mmol/L, respectively). Leftover-serum was frozen and tested retrospectively together with three test serum samples. Two were spiked with sodium formate to 20 mmol/L and 3 mmol/L, whereas one control contained no formate. All four samples (patients plus three test samples) were then blinded and presented separately to four intensive care doctors and two intensive care nurses for individual evaluation.
Results: The 20 mmol/L samples were identified as "high positive" by 6/6 test persons, the 3 mmol/L samples as "low positive" by 6/6, the control samples as "negative" by 5/6, and the patient sample as "negative" by 6/6. The patient sample was confirmed negative by the same GC-MS method as mentioned above.
Conclusion: In the present pilot study, all 6 participants identified the samples where the corresponding patient would require treatment, whereas 11/12 negative samples were accounted for. It thus provides a quick and clear identification of all patients with positive formate and thus symptoms likely caused by methanol poisoning. The falsely positive methanol test of our patient could have been eliminated bedside as a cause of acidosis if the strips were used on arrival.

205. Bedside quantitative electroencephalographic monitoring using the Patient State Index correlates poorly with Glasgow Coma Score in acutely poisoned patients

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Objective: Although the Glasgow Coma Scale (GCS) is frequently used to quantify conscious state in poisoned patients, GCS was originally derived in head-injured patients [1]. GCS in sedated poisoned patients correlates poorly with presence or absence of airway reflexes. Bedside electroencephalographic monitoring using the Patient State Index (PSI), an algorithm-derived analogue quantitation of sedation (range 0-100), has proven utility in general anesthesia [2]. A PSI value of 25-50 is considered optimal for surgical anesthesia. PSI may be useful in quantifying sedation in poisoned patients. As an initial step in assessing the utility of PSI we examined the correlation between GCS and PSI in Emergency Department patients with sedative drug poisoning.
Methods: A prospective observational study in a convenience sample of adult patients (>16 years) presenting to a tertiary-level metropolitan Emergency Department with an initial GCS <13 following sedative drug poisoning were monitored using a bedside PSI-based electroencephalographic monitor. Patient demographics, exposure history and serial physiological indices including GCS and PSI readings were recorded.
Results: One-hundred and fifteen separate GCS-PSI measurements were obtained in 28 patients, with median age 41 years (range 20-94). Half the patients were female. Median presentation GCS was 6 (range 3-13) and mean presentation PSI was 69 (range 16-95). Common exposures included antipsychotics, antidepressants, benzodiazepines and gamma-hydroxybutyrate (GHB). Overall, there was poor correlation ($R^2 = 0.1532$) between the 115 GCS-PSI paired measurements. Seven patients had a GCS of 3 during monitoring, with 26 concurrent PSI readings obtained (median PSI 53, range 16-93, IQR 28-80). PSI was >80 in 35% (9/26) of instances when concurrent GCS =3. PSI ranged from 70-92 for the 25 measurements obtained in patients with a GCS of 13 or 14 [IQR 82-89]. Study numbers were too small to make conclusions regarding GCS-PSI findings for specific drug classes. This study did not examine the relationship between PSI and airway reflexes in poisoned patients.
Conclusion: Overall, there was poor correlation between GCS and PSI in ED patients sedated secondary to poisoning. GCS-PSI correlation was superior for sedative states with GCS 13-14, compared to GCS 3. Further study is required to understand the relationship between bedside electroencephalographic findings, conscious state and airway reflexes in poisoned patients.

References

[1] Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet. 1974;2:81–84.
[2] Lee KH, Kim YH, Sung Y, et al. The Patient State Index is well balanced for propofol sedation. Hippokratia. 2015;19:235–238.

206. Hypotension in poisoned patients: the key role of echocardiography in differential diagnosis and management

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Objective: Hypotension is one of the most frequent symptoms in poisonings. A variety of pathologies may cause it, the shock may be multifactorial, and its therapy is often specific. The four core

Table 1. Characteristics of poisoned patients with hypotension (blood pressure <80/50 mmHg) showing the number with treatment adjusted depending on the cause of the hypotension.

		Early hemodynamic profile					
Type of poisoning	Number of patients	Normal	Cardiogenic	Hypovolaemic	Obstructive	Vasoplegic	Number of modified or upgraded initial therapy
Benzodiazepines	6	2	1	2	0	1	2
Barbiturates	1	0	1	0	0	1	0
Anticonvulsants	4	1	1	2	0	0	2
Antidepressants	14	1	5	5	1	6	6
Antipsychotics	6	1	2	2	1	1	2
Tolperisone	1	0	0	0	0	1	0
Tizanidine	1	0	1	0	0	1	0
Rilmenidien	5	0	5	2	0	1	2
Moxonidine	1	0	1	0	0	1	0
α_1B	8	0	0	1	0	8	1
Nitrates	9	0	0	0	0	9	0
ACEI, ARB	6	1	0	1	0	4	1
Drotaverine	2	0	0	0	0	2	0
Sildenafil	1	0	0	0	0	1	0
NaCB	2	0	2	0	0	0	0
BB	17	1	14	2	0	2	2
CCB	31	0	16	4	0	31	0
Digoxin	1	0	0	1	0	0	1
Methylxanthines	3	0	0	2	0	2	0
Alcohol only	6	0	1	3	0	2	1
Drugs of abuse	27	8	2	14	1	8	8
Other toxins	8	0	3	3	0	2	0
Total	**160**	**15**	**55**	**44**	**3**	**84**	**28**

α_1B: alpha$_1$-adrenergic receptor blockers; ACEI: angiotensin-converting enzyme inhibitors; ARB: angiotensin II receptor blockers; NaCB: sodium channel blockers; BB: beta-adrenergic receptor blockers; CCB: calcium channel blockers.

types and the leading and concomitant mechanisms of shock can readily be identified by echocardiography (echo) allowing modification of initial therapy. We evaluate the early hemodynamic profile of poisoned patients presenting with hypotension to our department and determine the role of point-of-care echocardiography in differential diagnosis and guiding treatment.
Methods: In a 1.5-year retrospective study we collected the demographic, clinical and echo data of patients presenting to our department with a blood pressure less than 80/50 mmHg even after a fluid loading of 500 mL along with the suspicion of acute overdose. The cases where the diagnosis of poisoning could not be confirmed or those with known cardiac dysfunction were excluded. The echo parameters were determined by a cardiologist or well-trained intensivist or emergency physician. Hemodynamic disturbances were divided into 4 groups: hypovolaemic (inferior vena cava diameter <10 mm and an increase in stroke volume >12% after passive leg raising), vasoplegic (reduced systemic vascular resistance), cardiogenic (reduced stroke volume) and obstructive (unequivocal signs of cardiac tamponade, dynamic left ventricular outflow tract (LVOT) obstruction or pulmonary embolism).
Results: In 25.6% of the cases more than one cause of hypotension could be identified and in 17.5% the initial therapy was modified and/or upgraded based on echo findings (Table 1).
Conclusion: Our data suggest that in acute intoxications hypovolaemia is a frequent and often overlooked complication and that hypotension caused by poisoning is frequently multifactorial. Also, depending on echocardiographic findings modification of the initial therapy can be life-saving. Echocardiography as a non-invasive and easily accessible method is essential in the correct diagnosis and management of poisoned patients with marked hypotension.

207. A one-year retrospective study of caustic injury in adults admitted to a toxicology department

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Objective: To present the results of a one-year clinico-epidemiological investigation of caustic injury in adults.
Methods: The study includes 16 patients with acute corrosive ingestion, hospitalized in the Toxicology Clinic, UMHATEM "N.I. Pirogov", Sofia, Bulgaria for the period 1 January to 31 December 2018. We collected data on gender, age, suicidal intention, previous history of severe mental illness, clinical course, therapy and outcome. The methods used include: clinical observation and examination, clinical laboratory, and imaging methods.
Results: Overall 16 patients between the ages of 29 and 92 years with acute corrosive ingestion were admitted in the study period. Ten were male (62.5%) and six female (37.5%). In nine cases (56.3%) ingestion was intentional, and accidental in seven patients (43.8%). Alkaline agents were involved in all cases. The severity of poisoning varied from moderate to extremely severe. After caustic ingestion all our patients complain of painful and burning mouth and throat, retrosternal chest and stomach pains, nausea, and vomiting. We observed also sialorrhea, difficulty in swallowing with edema, ulceration or whitish plaques in the oral cavity, palatal mucosa and pharynx. For injury staging, we used upper gastrointestinal endoscopy 24–48 hours after ingestion. Most patients had grade 2 injuries. Treatment included parenteral hydration and nutrition, H_2-receptor antagonists or proton pump inhibitors, steroids, antibiotics, analgesics, spasmolytics, and sedatives. A fatal outcome was registered in one patient. In the other patients acute complications were not registered. No patients required surgical intervention. The motivation for corrosive ingestion was also studied. Psychiatric comorbidity occurred in some of the patients: a background history of depression featured in two cases, schizoaffective disorder in two cases, harmful use of alcohol in five, behavioral and mental disorders due to the use of amphetamines in one patient, as well as an existential crisis in one case.
Conclusion: Corrosive ingestion is a serious medical problem in Bulgaria. The results from our study confirm the data known from the literature and from the practice of other countries.

208. Message on the bottle: how does the wrong package influence occurrence of caustic and corrosive chemical exposures – the Estonian experience

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Objective: Caustic and corrosive exposures are a worldwide problem. In Estonia caustic exposures cost the national health insurance system about 25,000 € every year. This retrospective study aims to collect epidemiological data about caustic and corrosive oral exposures in Estonia and establish the role of the substance not being in its original package in causing exposures in different age groups.
Methods: Calls to the Estonian Poisons Information Centre (EPIC) from January 2009 to December 2018 were analysed retrospectively in 6 age groups: under 1 year old, 1-3 years, 4-6 years, 7-18 years, 19-69 years and 70 years and older. For each group the following information was collected: whether the substance involved was caustic (pH ≤2 or ≥11.5) or irritating (pH 2-11.5), whether the product was in its original package and whether the patient needed to be hospitalized or was referred for home observation.
Results: Overall 1661 enquiries were registered. Exposures to caustic and corrosive chemicals were most common in children from 1 to 3 years (50.5% of all enquiries). This group was also most commonly asymptomatic or presenting only mild symptoms (80% referred for home observation, overall 79%). Overall, irritating substances were involved in 72% of exposures and caustic substances in 28%. Caustic exposures occured most often in patients older than 70 years (57%), and was lowest in patients younger than 1 year (16%). The chemicals were in their original package in 47% of cases; most often in the group aged 1-3 years (66%), and most rarely in the group aged 19-69 years (14%). The products were in another container in 30% of cases; 67% in the group aged 19-69 years, 62% in children aged 7-8 years, and only 8% in 1-3 year old children. The packaging was unknown in 23% of cases.
Conclusion: Results of the study show that cases involving products in containers, other than their original packaging, involve adults and older children, while children under 3 years old were more attracted by colorful original packages and products resembling or mistaken for toys (e.g. detergent pods, toilet fresheners). Surprising, most cases in children under 1 year of age involved the original packaging (51%). Probably it would be different if we examined cases involving children under and over 6 month olds in separate groups. Having such data helps the EPIC to target our prevention work for different age groups.

209. Pediatric ingestion of caustic drain cleaners

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Objective: Oral caustic exposure to drain cleaners is a public health event. Accidental oral exposures to drain cleaners reported to an Italian Poison Control Center from 1 November 2017 to 31 October 2018 were analyzed. There were 35 cases during the study period. Among them, 42.9% of cases involved children <6 years old. The present contribution is aimed at describing two pediatric cases with severe oral effects and gastroesophageal lesions due to ingestion of drain cleaners.
Case series: A 21-month-old girl ingested a sodium hydroxide-based (25-30%) drain cleaner left on the floor by her mother. She opened the bottle very easily and drank the pink liquid, mistaking it for a drink. On arrival to hospital, 15 minutes after ingestion, she presented second degree burn of 10% of the body surface. Oral examination showed first and second degree burns, disepithelization of the lips and necrosis of the oral cavity with blackish secretions from the mouth. Laryngoscopy revealed epiglottic edema. Gastroscopy found esophageal stenosis and erosions. She was intubated and subjected to multiple esophageal dilations. A 21-month-old boy ingested a sulphuric acid-based (75-100%) pink colored, drain cleaner, left on a shelf accessible to children at his mother's friend's house. He was found vomiting with the colored bottle next to him. He was admitted to the emergency room with dyspnea, dysphonia, edema of the oral cavity, epiglottic edema, disepithelization of the lips, necrosis the oral cavity, and hematemesis. Chest X-ray showed an opacity. Gastroscopy found severe esophageal and gastric erosions and he required endotracheal intubation.
Conclusion: Despite the presence of the safety closures on the bottle and the hazard pictograms on the packaging, the risk represented by these products is underestimated not only in adults but also in children.

210. False positive result on colorimetric methanol screening test: report of two cases with hyperglycaemia

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Objective: Tests for definitive detection of methanol in poisoning cases are not always readily available in hospital settings. The initial screening test may give a false positive result. Here, we report two cases with false positive colorimetric screening tests, leading to unnecessary treatment with fomepizole.
Case series: Case 1. A 48-year-old lady with history of schizophrenia and multiple substance abuse presented with acute vomiting, diarrhoea and impaired consciousness for 1 day. Examination revealed altered sensorium (Glasgow Coma Score [GCS] 7), severe dehydration and acidotic breathing. Severe metabolic acidosis and hyperglycaemia were noted on admission to the intensive care unit (ICU) (pH 6.72, PCO_2 1.58 kPa, PO_2 19.27 kPa, base excess -34 mmol/L; plasma glucose 49.9 mmol/L). Whole blood beta-hydroxybutyrate concentration was elevated (4.9 mmol/L). The anion gap (AG) and osmol gap (OG) were 43 mmol/L and 19.5 mOsm/kg, respectively. Lactate and chloride concentrations were normal. Serum ethanol and salicylates were undetectable. Intravenous insulin and fluid infusion were commenced for management of diabetic ketoacidosis. As an initial evaluation of high-anion gap metabolic acidosis, the colorimetric methanol screening test result was positive and fomepizole and continuous veno-venous haemofiltration (CVVH) were initiated. Subsequent confirmatory analysis by gas chromatography with flame-ionisation detection (GC-FID) was negative for methanol in serum and urine. Case 2: A 78-year-old man with chronic alcoholism presented with impaired consciousness after drinking alcohol of unknown origin. Examination revealed low blood pressure (60/40 mmHg) despite fluid resuscitation and dopamine infusion. Investigations revealed severe metabolic acidosis (pH 6.81, PCO_2 5.7 kPa, PaO_2 4.0 kPa, base excess -27 mmol/L), hyperglycaemia (plasma glucose 16.3 mmol/L), and elevated whole blood lactate (14.1 mmol/L). Whole blood beta-hydroxybutyrate was not elevated. The AG and OG were 50 mmol/L and 41.4 mOsm/kg, respectively. Serum salicylate and ethanol were undetectable. A serum methanol screening test was positive. The patient was treated with fomepizole and CVVH in the ICU. Again, methanol could not be detected by GC-FID.
Conclusion: The colorimetric methanol screening test employs chromotropic acid to detect formaldehyde formation in the presence of methanol, and acidified potassium permanganate and sulphuric acid as reagents. It is known the colorimetric methanol screening test detecting formaldehyde formation can be limited by false positives. Of note, the presence of glucose in the specimens may explain the interference [1]. Our two patients with hyperglycaemia highlight the importance of awareness of laboratory interference leading to misinterpretation and unnecessary treatment.

Reference

[1] Houle MJ, Powell RL. A modified chromotropic acid method of glucose analysis. Anal Biochem. 1965;13:562–565.

211. The value of post-mortem toxicology in deciding whether a death is drug-induced

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Objective: Post-mortem toxicological analysis examines biological samples of the deceased to determine the presence and concentration of poisons. However, there are serious difficulties in interpreting the findings. There is no reliable connection between concentrations measured in life and subsequent to death. Coroner's cases where toxicological samples have been taken, were examined to establish whether, in clinical terms, the death can be classed as DID (drug-induced death) or DID-not (not drug-induced).
Methods: Post-mortem toxicology data, along with brief clinical and demographic details, were selected at random from cases referred from two HM Coroners, serving North Wales. Two clinical toxicologists, initially blinded from the post-mortem toxicology report, examined the data and assigned a probability to the classification of DID (>50% certain) or DID-not (≤50%). The correlation between the quantitative toxicological findings, the

assessments of DID or DID-not, and the inquest findings (death certificate) was determined. Data was analysed using descriptive statistics, Cohen's coefficient and chi-squared. An alpha of <0.05 was considered significant.
Results: Twenty-six out of 32 cases had death certificate data available at the time of analysis. Of these 26, the median age at time of death was 47 years (range 19 to 87 years) with 17 males and 9 females ($p = 0.12$). Seventy-three chemicals were identified during post-mortem toxicology blood analysis. The median number of chemicals identified per case, during post-mortem toxicology blood analysis was 3 (range 0-7). Post-mortem blood was positive for ethanol in 14 cases (54%), median concentration 150 mg/dL, range 6-253 mg/dL. Opiates were detected in 22 cases (32%), benzodiazepines or Z-drugs in 11 cases (16%), antidepressants in 9 cases (13%), antipsychotics in four cases (6%), non-opioid analgesics in four cases (6%), cocaine in 3 cases (4%) and amphetamines in 2 cases (3%). The agreement between the two Clinical Toxicologists was assessed as "good" (Cohen's coefficient 0.90). The clinical toxicologists concluded that the death was a DID in 10 cases, DID-not in 13 cases and there was insufficient data to comment in three cases. Two cases (8%, 95% CI 1% to 25%) assessed as DID by the Clinical Toxicologists did not record a drug on the death certification.
Conclusion: Demining if a death was drug-induced, even with evidence of drug exposure, is not straightforward. Clinical Toxicologists appear to have good agreement in determine DID and may contribute to toxicology data interpretation.

212. Laboratory variability in reporting salicylate levels may limit high-quality poison center recommendations

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Objective: Hemodialysis is indicated in severe salicylate poisoning, as defined by clinical status, high serum salicylate concentration, or both [1]. Occasionally, dialysis may be indicated based on concentration alone. Therefore, it is essential that toxicologists and poison specialists understand the laboratory capabilities of their referral institutions in order to provide treatment recommendations. Our goal was to assess how salicylate was measured and reported by hospital laboratories in a large metropolitan area covered by a regional poison center.
Methods: We electronically surveyed hospital laboratory medical directors within the New York City Poison Control Center catchment area to gather the following data on how they approach high serum salicylate concentrations: analyzer details (brand, model), highest reported pre-dilution salicylate concentration, dilution protocols, highest post-dilution salicylate concentration, and dialysis capabilities. We compared these data to analyzer-specific protocols from the manufacturer.
Results: At the time of submission, 21 hospital responses were recorded. Eighteen of 21 hospitals reported having inpatient dialysis services; 17 could measure serum salicylate concentration on-site. Six hospitals reported maximum pre-dilution concentrations of 5.1 mmol/L, 1 reported 6.5 mmol/L, and 10 reported 7.2 mmol/L. Fifteen hospitals performed dilutions on specimens with salicylate concentrations above the upper limit of their assay's reportable range: 8 automatic and 7 manual. All 10 hospitals with an initial maximum of 7.2 mmol/L diluted specimens. Two hospitals did not dilute despite manufacturer recommendations.
Conclusion: Although hemodialysis in salicylate toxicity is recommended for salicylate concentrations >7.2 mmol/L (or >6.5 mmol/L in conjunction with renal impairment) [1]; two laboratories did not provide concentration >5.1 mmol/L. Many laboratories relied on manual dilutions for high salicylate concentration specimens, thereby creating an opportunity for human error and delayed reporting. This in turn affects poison center recommendations. Additionally, 10 laboratories that perform dilutions on salicylate concentration >7.2 mmol/L have unclear utility as the threshold to perform dialysis has been reached. There are several limitations to our study. It was not designed to assess the impact on poison center recommendations based on high salicylate concentration. Also, compliance with the stated laboratory protocol was not investigated. Future research is needed to assess how these variations impact patient-centered outcomes.

Reference

[1] Juurlink DN, Gosselin S, Kielstein JT, et al. Extracorporeal treatment for salicylate poisoning: systematic review and recommendations from the EXTRIP workgroup. Ann Emerg Med. 2015;66:165–181.

213. Valproic acid reporting cutoffs impact poison control recommendations

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Objective: Valproic acid (VPA) toxicity causes metabolic and neurologic symptoms through impairment of fatty-acid metabolism and the urea cycle. While VPA is typically 90% protein-bound, this fraction may drop to 15% in the setting of massive overdose rendering the drug amenable to extracorporeal treatment (ECTR). Timely, accurate determination of very high VPA concentrations is required to identify patients who would most benefit from ECTR, which is recommended at concentrations of greater than 9,000 µmol/L.
Methods: We surveyed hospital laboratory medical directors within the New York City Poison Control Center catchment area on their institutional approach to very high serum VPA concentrations. Specific data collected included: analyzer brand, analyzer model, highest reported pre-dilution VPA concentration, dilution protocol, highest reported post-dilution VPA concentrations.
Results: Twenty-one of 51 hospital laboratory directors responded to the survey. The highest reported pre-dilution concentration was 2,882 µmol/L and the lowest reported without a protocol for dilution was 960.5 µmol/L. Thirteen hospitals were not able to determine the recommended level for hemodialysis of 9000 µmol/L.
Conclusion: It is critical to determine the VPA concentration in massive overdoses for poison centers to provide optimal recommendations. Unfortunately, most hospitals were unable to obtain values over 2079 µmol/L. Hospitals should be encouraged to develop protocols to obtain accurate and timely serum VPA concentrations, including at high concentrations. Poison centers should also understand the capabilities of their referral sites. Early transfer to a facility that can appropriately perform dialysis and measure VPA concentrations may be appropriate in patients with suspected massive overdose.

214. Precise determination of phenobarbital concentrations may delay patient-centred care in severe poisoning

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Objective: Hemodialysis is indicated in severe phenobarbital poisoning, as defined by a combination of clinical status and high phenobarbital concentrations [1]. Very occasionally, dialysis may be indicated based on concentration alone. Thus, it is essential that toxicologists and poison specialists understand the laboratory capabilities of their referral institutions in order to provide optimal treatment recommendations. Our goal was to assess how phenobarbital was measured and reported by hospital laboratories in a large metropolitan area covered by a regional poison center.
Methods: We electronically surveyed hospital laboratory medical directors within the New York City Poison Control Center catchment area to gather the following data on how they approach high serum phenobarbital concentrations: analyzer details (brand, model), highest reported pre-dilution phenobarbital concentration, dilution protocols, highest post-dilution phenobarbital concentration, and presence or absence of inpatient dialysis services. We compared these data to analyzer-specific protocols obtained directly from the manufacturer.
Results: At the time of submission, 21 of 51 hospital responses were recorded. Eighteen of 21 hospitals reported having inpatient dialysis services, of which 15 could measure serum phenobarbital concentrations on-site. Eight hospitals reported a maximum pre-dilution concentration of 258 µmol/L, 1 gave 310 µmol/L, and 6 stated 344 µmol/L. Eleven hospitals performed dilutions: 5 automatic and 6 manual. Post-dilution maximum range was 517-1722 µmol/L.
Conclusion: Dialysis is not indicated as first-line therapy in phenobarbital toxicity, and the phenobarbital concentration only plays a role in the face of failure of supportive care [1]. Obtaining the precise phenobarbital concentration is not necessary to guide poison center recommendations—especially if dilution is required as this may further delay timely supportive interventions. Additionally, outpatient use of phenobarbital has declined and overdoses have also fallen in incidence. Patients chronically taking phenobarbital are also susceptible to withdrawal if dialysis reduces the phenobarbital concentration. There are several limitations of this study. This study is not designed to assess the impact on poison center recommendations based on high phenobarbital concentration or if there is a threshold concentration above which dialysis is necessary. Also, compliance with the stated laboratory protocol was not investigated. Future research should examine how variable lab practices impact patient-relevant outcomes in phenobarbital poisoning.

Reference

[1] Mactier R, Laliberte M, Mardini J, et al. Extracorporeal treatment for barbiturate poisoning: recommendations from the EXTRIP Workgroup. Am J Kidney Dis. 2014;64:347–358.

215. Variations in the detection, reporting, and interpretation of low acetaminophen concentrations may lead to overtreatment

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Objective: When the timing of an acetaminophen (APAP) overdose is unknown, N-acetylcysteine (NAC) should be administered until the serum acetaminophen concentration falls to a low or undetectable level. Poison center recommendations rely on precise measurements of serum concentrations at the treating facility. Variations in laboratory measurement and reporting procedures for APAP at low concentrations may therefore affect patient care by altering the duration of NAC treatment. We analyzed laboratory protocols at hospitals across a large metropolitan area. Our objective was to identify the degree of local practice variation so that we might generate strategies to improve the care of acetaminophen-poisoned patients at the poison center level.
Methods: We surveyed hospital laboratory medical directors within the New York City Poison Control Center catchment area. Respondents provided values for the lowest acetaminophen concentration they report and details about their analyzers. Reporting cutoffs were compared to manufacturer-specified minimum-detectable concentrations for each laboratory's analyzer. For additional context, we examined the criteria for NAC cessation recommended by 5 reference texts (internal medicine, emergency medicine, medical toxicology), one toxicology professional society, one acetaminophen manufacturer, and one online point-of-care decision-support resource.
Results: At the time of submission, 21 of 51 hospitals had responded to the survey. Seventeen measure serum acetaminophen concentration. Quantified concentrations as low as 6.6 µmol/L are reported to clinicians by 1 hospital, 11 µmol/L by 2 hospitals, 13 µmol/L by 5 hospitals, 20 µmol/L by 1 hospital, 33 µmol/L by 4 hospitals, 53 µmol/L by 1 hospital, 66 µmol/L by 2 hospitals, and 99 µmol/L by 1 hospital. Whereas most hospitals reported all values within the measurable range of their analyzer, multiple hospitals used a higher reporting cutoff. For example, one hospital employs an analyzer capable of concentration quantification as low as 33 µmol/L, but reports all results less than 99 µmol/L as "< 99 µmol/L." The reviewed references recommended stopping NAC when serum acetaminophen concentration was <66 µmol/L (1 reference), when it was undetectable (4 references), or either (2 references). One reference did not establish objective cessation criteria.
Conclusion: Our findings demonstrate substantial variations in the measurement, reporting, and interpretation of low serum acetaminophen concentrations. We suspect that the reporting of detectable but physiologically insignificant concentrations increases the cost and duration of NAC therapy but future work is needed to determine the impact of different acetaminophen concentration reporting thresholds on patient-centered outcomes.

216. Laboratory practice variations complicate poison centre recommendations for massive paracetamol overdose

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Objective: Massive paracetamol (APAP) overdose is characterized by early-onset altered mental status, metabolic acidosis, and shock due to direct mitochondrial toxicity. Hemodialysis has shown promise as an adjunct to N-acetylcysteine, but the decision to dialyze depends on toxidrome recognition, nephrology consultation, and rapid access to accurate serum concentration measurements above 3300 µmol/L (500 mg/L) [1]. It is unclear whether modern laboratories are equipped to provide the latter. We examined institutional laboratory practice variations for high APAP concentration serum samples within the referral network of a large regional poison center. Our goal was to use these data to provide institution-specific poison center recommendations for suspected massive APAP overdose.
Methods: We surveyed 51 hospital laboratory directors in the state of New York to collect the following data: APAP analyzer brand and model, highest reported pre-dilution APAP concentration, dilution protocol, highest reported post-dilution APAP concentration, and availability of inpatient hemodialysis. We compared these findings to protocols outlined in analyzer-specific data sheets obtained directly from the manufacturer.
Results: Twenty-one of 51 hospitals responded (41%). Seventeen hospitals with inpatient dialysis services could measure APAP onsite and one could not. Maximum reported pre-dilution serum APAP concentration depended on the analyzer: 7 hospitals reported 1320 µmol/L (5 Roche Cobas, 1 Siemens ADVIA, 1 Siemens XPT), 8 hospitals reported up to 1980 µmol/L (3 Roche Cobas, 3 Siemens Vista, 1 Siemens ADVIA, 1 Beckman Coulter DxC), and 2 hospitals reported 2310 µmol/L (2 Abbott Architect). Maximum reported post-dilution serum APAP concentration could not be fully explained by analyzer variation and sometimes deviated from manufacturer recommendations: 1 hospital reported up to 1980 µmol/L, 9 reported between 1981-3960 µmol/L, 3 reported between 3961-6600 µmol/L, and 4 could quantify concentrations >6600 µmol/L.
Conclusion: Hospital laboratories are generally well-equipped to handle typical APAP poisonings but massive overdose presents a unique challenge to clinicians and laboratorians. The majority of surveyed hospitals were unable to quantify serum APAP concentrations above 3960 µmol/L. Our study did not characterize the time needed for sample dilution or real-world adherence to institutional protocol—factors that may further delay hemodialysis. Our poison center uses these data to facilitate early transfer, justify empiric hemodialysis, and guide discussions with laboratory technicians reluctant to perform serial dilutions. More interdisciplinary collaboration is needed to improve the care of patients with massive APAP overdose.

Reference

[1] Gosselin S, Juurlink DN, Kielstein JT, et al. Extracorporeal treatment for acetaminophen poisoning: recommendations from the EXTRIP workgroup. Clin Toxicol (Phila). 2014;52:856–867.

217. Poison center recommendations for severe lithium poisoning are limited by laboratory protocol variations

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Objective: Severe lithium toxicity may result in seizures, encephalopathy, and permanent neurologic sequelae. The Extracorporeal Treatments in Poisoning Workgroup (EXTRIP) recommends extracorporeal toxin removal (ECTR) in cases of severe lithium poisoning, as defined by clinical features, serum lithium concentration, or both [1]. Unfortunately, not every hospital laboratory can measure high lithium concentration. We studied how lithium was measured and reported in hospital laboratories across a large metropolitan area in order to improve poison center recommendations in this population.
Methods: We electronically surveyed hospital laboratory medical directors within the New York City Poison Control Center catchment area to gather the following data: highest reported pre-dilution lithium concentration, dilution protocols, highest post-dilution lithium concentration, analyzer details, and availability of inpatient hemodialysis. We compared these data to analyzer-specific protocols obtained directly from manufacturers.
Results: Twenty-one of 51 hospitals responded to the survey. Ten out of 21 institutions reported up to 3 mmol/L without further dilution. Eight hospitals reported pre-dilution levels between 3-7 mmol/L. Sixteen hospitals were able to extend the reportable range to at least 6 mmol/L with dilution. Two hospitals responded with maximum reportable concentrations of 4 mmol/L and did not perform dilutions. Seven hospitals performed autodilution and these protocols adhered to best practices per manufacturer data sheets. Three hospitals were unable to perform lithium concentrations, but these also did not have on-site dialysis capabilities.
Conclusion: ECTR is recommended for patients with lithium concentrations >4.0 mmol/L and impaired kidney function (or >5.0 mmol/L with no renal impairment) [1]. Despite the severe morbidity associated with lithium toxicity, nearly half of surveyed hospitals were unable to quantify lithium concentration >3 mmol/L without further dilution and two hospitals that measured up to 4 mmol/L did not perform any dilutions. It is critical to determine lithium concentrations in a timely fashion in patients with suspected toxicity for poison centers to provide optimal recommendations. Toxicologists and laboratorians should be encouraged to develop protocols to rapidly quantify high lithium concentration serum specimens.

Reference

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218. Poison center recommendations for methylxanthine toxicity may be complicated by limited access to theophylline measurements

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Objective: Severe theophylline toxicity may cause tachydysrhythmias, hypotension, refractory seizures, and death. Although theophylline is 56% protein-bound at therapeutic concentrations, it is readily removed by extracorporeal treatments (ECTR) [1]. The availability of timely serum theophylline concentration measurements may affect treatment recommendations and patient outcomes in severe toxicity. Our descriptive study characterized the theophylline-measuring capabilities of hospitals within the catchment area of a large regional poison center.
Methods: We surveyed hospital laboratory directors within the referral area of the New York City Poison Control Center, which covers a population of 14 million people. The survey gathered the following data: analyzer details, highest reported pre-dilution theophylline concentration, dilution protocol, highest reported post-dilution theophylline concentration, and availability of inpatient dialysis. We obtained analyzer-specific datasheets and compared reported dilution protocols to manufacturer recommendations.
Results: Twenty one of 51 hospitals responded to our survey. Eight hospitals (38%) did not perform the test in-house. Thirteen hospitals (62%) reported a maximum pre-dilution concentration of 40 mg/L and 1 (5%) reported 120 mg/L. Ten (48%) institutions reported a post-dilution maximum concentration of 80 mg/L, 2 (10%) reported 120 mg/L, and 2 (10%) hospitals did not dilute samples in contravention of manufacturer's guidelines and designated these results as ">40 mg/L".
Conclusion: Although clinical features must be considered in the risk assessment of acute theophylline toxicity, >100 mg/L has been independently associated with increased morbidity. Our results demonstrate that many New York laboratories lack the capacity to quantify very high theophylline concentrations associated with serious toxicity. Given the similarity of clinical symptoms below and above the 100 mg/L threshold, absence of an accurate theophylline concentration may affect the ability of poison centers to give optimal recommendations. Given that the therapeutic use of theophylline and routine theophylline concentration monitoring has been declining for decades [1], future interdisciplinary collaboration is needed to overcome this diagnostic limitation for patients with suspected methylxanthine overdose.

Reference

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219. Clozapine-induced anemia: a case report

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Objective: Clozapine, an atypical antipsychotic, can cause potentially life-threating side effects such as agranulocytosis. Our case presents a picture of severe anemia without any depression of the white cells or platelet lines. To our knowledge, few cases of clozapine-induced anemia have been reported.
Case report: A 36-year-old man with schizophrenia unresponsive to risperidone and paliperidone and an unremarkable medical history was admitted to the Psychiatric Unit for therapy reassessment. At admission, general laboratory test results were normal, with a hemoglobin (Hb) of 15.2 g/dL. He was gradually switched to clozapine treatment, 400 mg/day. The Hb gradually decreased and dropped to 8.1 g/dL 10 weeks after switching to clozapine, when the patient received a blood transfusion and clozapine therapy was stopped. No evidence of bleeding was noted. The reticulocyte count was less than 60,000/µL. The erythropoietin concentration was increased at 67 mU/mL (normal 2.6-34 mU/mL). Both direct Coombs test and antinuclear antibodies were negative. Tests for serum parvovirus B19 DNA and HIV yielded negative results. Iron tests showed ferritin concentrations of 564 ng/mL (normal 20-250 ng/mL) in the presence of a normal serum iron. Moreover, abdominal magnetic resonance imaging (MRI) showed almost normal hepatic iron overload of 36 µmol Fe/g tissue (normal <36 µmol Fe/g tissue) measured following the University of Rennes protocol, excluding hemochromatosis or a sideroblastic anemia. A chest radiograph excluded the presence of thymoma. Bone marrow aspiration performed at 10 weeks revealed red cell hypocellularity, while myelopoietic and megakaryocytic cell lines were normal. All these findings confirmed the diagnosis of pure red cell hypoplasia. The Hb gradually increased to 13.3 g/dL four weeks after clozapine discontinuation. The patient was discharged with olanzapine 5 mg/day.
Conclusion: Clozapine has been reported to cause agranulocytosis and other hematological abnormalities. In our patient the diagnosis of pure red cell hypoplasia was made on the basis of severe and selective anemia, reticulocytopenia and erythroid hypoplasia. The pathogenesis of hematologic abnormalities due to clozapine treatment is not known; suggested mechanisms include a direct toxic effect of clozapine, or its metabolites, on the erythroid precursor cells, or formation of a drug-antibody complex. Laboratory investigation has identified clozapine as exhibiting toxic effects against myeloid maturation. These aspects call for further and deeper research and reports of clinical observations. In the meantime, considering the severe anemia observed, a greater emphasis should be given to the clinical relevance of this adverse drug reaction.

220. Lacosamide-induced recurrent ventricular fibrillation

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Objective: Lacosamide, a new antiepileptic drug, acts at the central nervous system level but may also affect the heart, increasing the risk of cardiac arrhythmias. Few cases of lacosamide-induced cardiac dysrhythmia have been published. We report a case of several episodes of a life-threatening ventricular fibrillation requiring cardioversion following the first doses of lacosamide as adjunctive epilepsy treatment.
Case report: A 38-year-old female in a persistent vegetative status due to cerebral hemorrhage, with myocardial hypertrophy and hypertension and without prior dysrhythmias, was transferred to our hospital for a ventriculo-peritoneal shunt placement. Her medication regimen consisted of levetiracetam 1 g IV every 8 hours. The surgical procedure was uneventful but 12 hours later she developed sudden onset generalized tonic-clonic seizures. Intravenous valproate 400 mg every 8 hours infused over 1 hour was started, but the blood pressure decreased to 70/46 mmHg; moreover hyperammonemia 122 µmol/L (normal value 6-48 µmol/L) was recorded during valproate therapy. Therefore, the patient was switched to intravenous lacosamide 400 mg infusion 3 times/day. In the meantime, gastric retention was observed and domperidone 10 mg every 8 hours was started. After the second dose of domperidone the QTc interval increased from 460 ms to 503 ms and the drug was stopped. Magnesium and potassium concentrations were both within the normal range. Six hours after the last domperidone administration the patient received the third dose of lacosamide, but soon after an episode of ventricular tachycardia occured, followed by 27 episodes of life-threatening ventricular fibrillation requiring cardioversion at 200 J over the next 12 hours. Following discontinuation of lacosamide all cardiac conduction abnormalities resolved. The lacosamide concentration 48 hours after the last dose was 12.9 mg/L (normal 1.0-10.0 mg/L). Two months later, the patient was discharged from the hospital without further cardiac arrhythmias.
Conclusion: Lacosamide selectively enhances sodium channel slow inactivation in neuronal and cardiac cells and can cause cardiac arrhythmias. Moreover, patients with prolonged QTc interval are inherently at risk of reentrant arrhythmias that can lead to lethal ventricular fibrillation. In this report, we postulate the hypothesis that domperidone treatment increased the QTc interval of our patient, thus promoting lacosamide-induced cardiac arrhythmia. Considering the life-threatening cardiac dysrhythmia observed, a greater emphasis should be given to the clinical relevance of this adverse drug-drug interaction.

221. Plasma half-life of benzodiazepines and Z-drugs and risk of hospitalisation: an Italian nationwide retrospective study

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Objective: Benzodiazepines (BZD) and Z-drugs (ZD) are widely prescribed medicines [1] with several clinical uses. These medications are often used inappropriately [2], and this is associated with adverse events, which may cause emergency department (ED) visits [3]. The objective of the present study was to describe the characteristics of BZD and ZD-related adverse events leading to an emergency department visit and/or hospitalisation in Italy, focusing on the risk of hospitalisation based on BZD and ZD plasma half-life.
Methods: A retrospective multicentre study was performed. Ninety-two Italian EDs participating to the MEREAFaPS (Epidemiological Monitoring of Adverse Drug Reactions and Events in Emergency Room) Study were monitored between 1 January 2007 and 31 December 2018. Patients (all age groups) having at least one clinical manifestation related to BZD or ZD were included. Rates of ED visits and hospitalisation were calculated. Multivariate logistic regression was used to estimate the reporting odds ratios (RORs) of hospitalisation, adjusting for age, sex, Caucasian ethnicity, number of suspected drugs, presence of concomitant medications, and presence of concomitant conditions. Univariate linear regression was performed to evaluate the ROR of hospitalisation according to the plasma half-life of the suspected agents.
Results: Overall, multivariate logistic regression showed that the risk of hospitalisation was significantly higher for prazepam (3.26 [1.31-8.11]), flurazepam (1.62 [1.15-2.27]), and lorazepam (1.36 [1.15-1.61]). In the elderly, this risk was significantly higher for prazepam (3.98 [1.03-15.3]), and lorazepam (1.58 [1.19-2.11]). Agents with a plasma half-life ≥12 hours were associated with a significantly higher relative risk of hospitalisation (1.22 [1.05-1.41]). Parenteral and rectal formulations were associated with a lower risk of hospitalisation compared to oral formulations.
Conclusion: Our findings underlined the potential dangers in the use of BZD and ZD, and the importance of clinical judgment in determining the appropriateness of their prescribing. The study highlights the association between the use of agents with a plasma half-life ≥12 hours and a higher risk of hospitalisations. These results emphasize the dangers related to an underestimated inappropriate usage of BZD and ZD in Italy.

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222. Bleeding events due to warfarin therapy: how much does it cost?

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Objective: To evaluate the frequency, severity and indirect costs of bleeding events in patients on warfarin therapy.
Methods: The retrospective cohort study was performed using data of patients who attended the Republican Vilnius University Hospital during 2013-2018. Inclusion criteria were bleeding events which required hospitalization in patients on warfarin therapy with an International Normalization Ratio (INR) > 2 on

Table 1. Indirect economical cost comparison of management of patients on warfarin therapy (n = 456) comparing duration of hospital and ICU stay and number of transfusions between different bleeding sites.

	Site of haemorrhage				
Parameter (mean)	Gastrointestinal	Urogenital	Otorhinolaryngological	Intracerebral	Other
Hospitalization length (days)	7.59	5.02	5.76	14.93	8.28
ICU length (days)	1.92	0.71	0.59	5.96	0.82
RBC transfusion	3.02	0.66	0.69	1.02	1.17
Fresh frozen plasma (FFP)	1.44	0.85	0.27	0.75	0.58
Prothrombin complex concentrate (PCC) count	1.05	0.44	0.69	2.95	0.88

admission. Patients with comorbidities (e.g. cirrhosis, congenital coagulopathies) that could cause bleeding were excluded. Data was collected on age, gender, localization of bleeding, duration of hospitalization, laboratory analyses, management of bleeding events and outcome (died or survived).

Results: The study included 456 patients, with median age 78 years [36;97]. There were 220 men (47.8%) and 236 women (51.3%). The most common events were gastrointestinal bleeding (n = 190, 41.6%), bleeding from nose or throat (n = 74, 16.2%) and intracerebral haemorrhage (n = 73, 16.0%). Bleeding from two different sites occurred in 41 cases (8.9%), and in 3 different sites in 2 patients. Major bleeding occurred in 280 cases; 207 patients had at least two red blood cell transfusions and 73 had intracerebral bleeding. Warfarin-induced haemorrhage was lethal in 67 patients (14.7%). The median duration of intensive care unit (ICU) stay until death was 3 days. Indirect economic costs of warfarin-induced bleeding events were determined (Table 1). Intracerebral bleeding caused the longest hospitalization and ICU stay, required the highest doses of prothrombin complex concentrate (PCC) (possibly due to the need for further surgical intervention). Gastrointestinal bleeding required high doses of transfusions (fresh frozen plasma (FFP) and red blood cells), although hospital stay was half, and ICU stay 3 times lower than in intracerebral bleeding cases. Overall 46.3% of patients required RBC transfusions.

Conclusion: The most common origin of bleeding was gastrointestinal and intracerebral. Intracerebral bleeding caused the longest hospitalization and ICU stay, and required the highest doses of PCC compared to other haemorrhage sites.

223. Phenytoin intoxication associated with omeprazole administration in a child with CYP2C9 polymorphism

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Objective: Phenytoin is a widely used antiepileptic drug, recommended to decrease the incidence of early post-traumatic seizures, which can cause severe adverse drug reactions at supratherapeutic plasma concentrations. Phenytoin metabolism is largely mediated by the cytochrome-P_{450} isoform, CYP2C9. CYP2C19 accounts for a minor component of phenytoin metabolism. The gene encoding for CYP2C9 is polymorphic, and the allelic variants, CYP2C9*2 (rs1799853) and CYP2C9*3 (rs1057910), are associated with a reduced enzymatic activity. We present a case of toxicity resulting from a genetic polymorphism.

Case report: A 5-year-old child was admitted to the hospital for severe head trauma and transferred to the pediatric intensive care unit (PICU). Intravenous phenytoin (5 mg/kg, twice daily) and omeprazole (0.8 mg/kg, once daily) were started. No neurological deficits appeared in the first 3 days. At day 10, 2 days following phenytoin withdrawal, the child was awake but with loss of awareness and alertness, and horizontal nystagmus. Central neurological hyperventilation and bilateral Babinski sign were present. Phenytoin plasma concentrations were in the upper limit of the therapeutic range (20-21 mg/mL) in the first 4 days of administration, but increased afterwards and remained abnormally high (>35 mg/mL) 5 days after phenytoin withdrawal. At this time we suspended omeprazole administration, and phenytoin concentrations sharply decreased in the following 3 days, with a concomitant improvement of all neurological signs. Next Generation Sequencing analysis revealed the child had the homozygous variant c.1075A > C (p.Ile359Leu) of *CYP2C9*, corresponding to *CYP2C9*3* (rs1057910).

Conclusion: Omeprazole competes with phenytoin for CYP2C19-mediated metabolism, causing small changes in phenytoin plasma clearance (15% reduction) and elimination half-life (27% increase) in rapid phenytoin metabolizers [1]. Also, omeprazole may compete with phenytoin for plasma proteins binding, further contributing to phenytoin toxicity. Our findings suggest that proton pump inhibitors should be avoided in combination with phenytoin in children with defective CYP2C9 metabolism.

Reference

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224. Two cases of opioid withdrawal syndrome precipitated by alcohol dependence treatment with nalmefene successfully treated with morphine

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Objective: We present two patients on methadone maintenance therapy who developed opioid withdrawal syndrome after a single dose of nalmefene and were successfully treated with morphine. Nalmefene is an opiate derivative used in the management of alcohol dependence in adult patients who have a high drinking risk level. It acts as a competitive antagonist of the μ-opioid receptor and the δ-opioid receptor and as a weak partial agonist of the κ-opioid receptor. It is rapidly absorbed after a single oral administration with a peak concentration after approximately 1.5 hours. The terminal half-life is estimated as 12.5 hours [1].

Case reports: Case 1. A 33-year-old man on methadone maintenance treatment was admitted to the emergency department after ingestion of a single dose of 18 mg nalmefene. At presentation he suffered acute opioid withdrawal with intense agitation, abdominal pain, diarrhoea and tremor. After transfer to the intensive care unit he was treated with intravenous morphine with a loading dose of 50 mg and a continuous infusion of 700 mg per 24 hours over one day. The next day the morphine infusion was discontinued, methadone was restarted and the patient recovered without sequelae after one day in a medium care ward. Case 2. An adult drug addict under methadone maintenance therapy with a dose of 35 mg per day was prescribed nalmefene for alcohol dependence by his general practitioner. After a single dose of 18 mg nalmefene he became very thirsty and required hospitalization urgently for acute opioid withdrawal syndrome with intense agitation, abdominal pain and diarrhoea. He was treated with a loading dose of 15 mg of morphine and an infusion of 10 mg per hour for the next 24 hours. He recovered without sequelae.
Conclusion: Drugs for alcohol dependence should be prescribed guardedly and with a full understanding of their interactions with other medications in patients on methadone maintenance therapy. In these two cases the management of the precipitated acute opioid withdrawal syndrome after a single dose of nalmefene included the use of morphine for 24 hours in addition to supportive treatment during hospitalization.

Reference

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225. Incidence of adverse reactions after the administration of Taiwanese snake antivenoms: a review of 968 cases from 2001 to 2017

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Objective: Bites from Taiwan venomous snakes are life-threatening emergencies which require administration of anti-haemorrhagic antivenom (FH) and/or anti-neurotoxic antivenom (FN). Data on the safety profile of these Taiwanese-manufactured antivenoms, however, is limited. While these antivenoms are life-saving antidotes, they may also give rise to immediate hypersensitivity reactions (allergic reactions within 3 hours of administration) and serum sickness (adverse reactions 1-12 days after administration). Here, we investigate the incidence and risk factors of such reactions following the administration of FH and FN.
Methods: This study was mainly conducted using Chang Gung Research Database (CGRD), one of the largest multi-institutional electronic medical record systems for real-world epidemiological studies in Taiwan [1]. The prevalence rate and epidemiological characteristics of patients who developed allergic reactions were described. Univariate analyses and subsequent logistic regression analysis were used to evaluate the differences between patients with and without antivenom reactions.
Results: Out of 8,295,497 snakebite patients admitted to the emergency departments (EDs) of the 7 CGRD hospitals from January 2001 to May 2017, 968 patients received snake antivenom. Among them, 61.6% received FH, 18.7% patients received FN, and 19.6% received both FH and FN due to unidentified snakebites. In total 127 patients (13.1%) had adverse reactions, 91.3% of which were immediate hypersensitivity reactions, with life-threatening anaphylaxis accounting for 21.3%, and the remaining 8.7% being serum sickness. The incidences of antivenom reactions to FH, FN, and FH + FN were 12.2%, 12.7% and 16.3%, respectively. Most patients (96.9%) were managed in the emergency department (ED) observation ward or general ward. There were no cases of significant morbidity from antivenom administration. Administration of more than 4 vials of antivenom was determined to be the predictor of adverse reactions (odds ratio, 1.62; 95% confidence interval, 1.05-2.5).
Conclusion: Antivenoms manufactured in Taiwan can be used safely to treat bites from venomous snakes due to the relatively low incidence of adverse reactions, especially serum sickness. The majority of such patients can be managed safely in the ED observation ward or general ward. The risk of adverse reactions should be taken into consideration especially in patients receiving more than 4 vials of antivenom.

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226. Olanzapine overdose-induced agranulocytosis

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Objective: We report a case of agranulocytosis in acute olanzapine overdose.
Case report: A 55-year-old male with a history of psychosis, was admitted 10 hours after ingestion of approximately 350 mg of olanzapine. He was previously healthy, treated with 15 mg of olanzapine daily for two years and had not had previous antipsychotic-induced neutropenia episodes. On admission his mental status was fluctuating from stupor to somnolence with periods of agitation. He was afebrile, pupils were normal, heart rate 130/min, blood pressure 95/65 mmHg and oxygen saturation was 93%. No ECG abnormalities were detected. White blood cell (WBC) and neutrophil counts at admission were 3.04×10^9/L and 2.57×10^9/L, respectively. Creatine kinase (CK) was 10127 U/L with normal parameters of renal function and electrolytes. The olanzapine serum concentration at admission was 0.40 mg/L (toxic >0.15 mg/L). Initial therapy included fluids, benzodiazepines, bicarbonate and diuretics. Twenty four hours after ingestion, he was febrile and dyspnoeic, and in respiratory failure. He was sedated, intubated and mechanically ventilated for the next 6 days. Chest radiography showed bilateral consolidations. WBC and neutrophils had dropped to 0.47×10^9/L and 0.36×10^9/L, respectively. Antibiotics for febrile neutropenia were started and granulocyte colony-stimulating factor (G-CSF) was administered

for two days. The WBC and neutrophils on day 3 were 1.78×10^9/L and 1.40×10^9/L, respectively, and the day after were in normal ranges. Olanzapine serum concentrations were high for 6 days (0.56 mg/L on day 2, 0.42 mg/L on day 3 and down to 0.25 mg/L on day 6). He stabilised with aggressive support measures with clinical and radiographic regression of inflammation and recovery of consciousness. He was extubated on day 7. The CK value was normal on day 8. The patient completely recovered and was transferred to the psychiatric department 12 days after admission.
Conclusion: Olanzapine-induced neutropenia is a rare and potentially dangerous adverse effect during treatment with olanzapine, but not described in acute overdose [1]. In our case, this effect had a dose-related component and seriously influenced the poisoning severity and emphasizes the importance of WBC monitoring in acute poisonings. Also, increased CK activity recorded in our patient confirmed olanzapine muscular toxicity.

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227. From kitchen to clinical use, to emergency department admission: an Italian story about curcumin

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Objective: Curcumin is one of the molecules contained in the spice turmeric (*Curcuma longa*). It is a promising herbal remedy used for joint arthritis, type 2 diabetes, and dyslipidemia due to its antioxidant and anti-inflammatory activities, however, the systemic bioavailability of curcumin is known to be poor [1]. In Italy, during the past 6 months, an outbreak of acute non-infectious cholestatic hepatitis, including severe cases, has occurred, and these events have been related to the consumption of turmeric-based dietary supplements manufactured by various producers with 95% curcumin content. Of the 7 cases recorded in the Tuscany Region in 2019 we describe those directly observed by the Toxicology Unit of Careggi University Hospital.
Case series: Case 1 was a 57-year-old woman with right-upper quadrant abdominal discomfort, dark urine, nausea, asthenia and hyporexia. The patient reported taking a turmeric-based dietary supplement for 10-15 days before onset of symptoms. Abdominal ultrasound demonstrated mild liver steatosis. Blood tests showed hyperbilirubinemia (3.9 mg/dL) and elevated transaminase (ALT 2360 U/L). Case 2 was a 46-year-old woman with colicky, lower abdominal pain, changes in bowel habit and dark urine. The patient reported taking a turmeric-based weight loss product for 2 months up to 6 days before admission and was concomitantly undergoing treatment with paroxetine and alprazolam. Blood tests showed elevated ALT and cholestatic markers. Case 3 was a 57-year-old man hospitalised for severe mitral-aortic insufficiency that required surgery. The patient reported taking turmeric-based dietary supplements prior to hospital admission. During hospitalisation blood tests showed a progressive increase in liver function markers (ALT 3,303 U/L, AST 7,883 U/L) and kidney function markers. He was concomitantly being treated with amiodarone and azithromycin. All three patients were treated with N-acetylcysteine and showed normalisation of liver function within two months.
Conclusion: In all three cases, in the absence of other plausible causes of acute hepatitis (negative laboratory results for hepatotropic viruses and autoimmune hepatitis markers), curcumin in the form of dietary supplement could not be ruled out as a cause of acute non-infectious cholestatic hepatitis. All the dietary products responsible for acute hepatitis were tested by the Italian Ministry of Health and were found to be negative for contaminants. An alert was issued to advise consumers to seek advice from a physician whenever they considered taking a dietary supplement. Overall, an idiosyncratic reaction to curcumin could be hypothesized.

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228. Accidental injection of a pseudorabies pig vaccine in humans

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Objective: Pseudorabies virus, a member of the herpes virus group, causes Aujeszky's disease (pseudorabies) in pigs. The susceptibility of man to pseudorabies virus is controversial and single cases are reported [1], but Aujeszky's disease is considered non-transmissible to humans. Suvaxyn Aujeszky 783 + O/W® is a veterinary medicine administered for active immunization of pigs to prevent Aujeszky's disease. The product comprises a powder (live attenuated Aujeszky's virus), solvents (aluminium hydroxide, mineral oil, mannide mono-oleate and polysorbate-80), and excipient (thiomersal). We describe four cases of accidental injection in humans.
Case series: Cases of accidental human injection of Suvaxyn Aujeszky 783 + O/W® referred to the Pavia Poison Control Centre from 2014-2019 were retrospectively evaluated. Four patients (age 45 ± 11 years; male 75%) were evaluated. In all cases, patients accidentally self-injected (3 in the fingers, 1 in the knee) a residual dose of vaccine during administration to pigs. All 4 patients developed a local reaction with a pomphoid lesion at the injection site. In two cases, local clinical manifestations improved within 12 hours of symptomatic treatment. Two patients manifested severe asthenia associated with abrupt appearance (1 hour after injection) of fever (37.8 and 39.7 °C). In both cases blood tests were normal except for leukocytosis with normal procalcitonin. Hyperthermia improved after 24 hours with antipyretics and without antibiotic administration.
Conclusion: In case of human injection, the European Medicines Agency (EMA) product information reports the risk of local inflammation due to mineral oil. A transient increase in body

temperature, up to 40.5 °C and lasting for up to 2 days, is described as an acute adverse reaction in a small number of pigs after vaccination. In our experience hyperthermia could also occur in exposed humans and is probably due to a systemic inflammatory reaction related to the mineral oil. No patients developed the zoonosis. Workers and health professionals should be aware of this specific risk. A revision of the product characteristics including the risk of hyperthermia in humans after accidental injection is suggested.

Reference

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229. Bowel perforation due to methotrexate therapeutic error: a case report

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Objective: Methotrexate (MTX) is widely used in the treatment of some autoimmune diseases. Adverse effects are often associated with therapeutic errors such as the daily intake rather than weekly intake, especially when the drug is self-administered. Among the adverse effects of MTX, the risk of bowel perforation is extremely rare (0.1%) [1,2]. We describe a case of bowel perforation following daily intake of MTX.
Case report: A 68-year-old man was prescribed MTX 7.5 mg per *os* once a week, while waiting to switch to abatacept for a recent reactivation of rheumatoid arthritis. After 10 days, he started having pharyngodynia, haematochezia and general malaise. At medical examination he presented oral and nasal mucositis and thrombocytopenia. The history revealed that he had taken the prescribed dosage of MTX daily, instead of weekly. The MTX serum concentration was within the normal range, and immediate therapy with folinic acid 1000 mg (mg/m^2/day) and urinary alkalinisation was started. After 7 days later, the patient worsened abruptly. An emergency computerised tomography (CT) scan revealed millimetric gas bubbles indicating bowel perforation. The patient underwent an emergency exploratory laparotomy that resulted in peritoneal toilette and sigma resections. Anatomopathological findings were suggestive of MTX poisoning. The patient was discharged 17 days after admission in good clinical condition with planned rheumatologist controls for therapy management.
Conclusion: MTX-related bowel perforation, although potentially lethal, is rarely described in literature [1]. It is appropriate to consider that there is individual susceptibility and genetic predisposition for development of MTX adverse effects [2]. Furthermore, steroid therapy and/or a pre-existing diverticulitis disease, must be considered as risk factors for bowel perforation during MTX therapy [3]. All this should be taken into account during medical treatment with MTX.

References

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230. Toxicokinetics of diazepam after high dose administration for the treatment of ethanol withdrawal in a geriatric patient: how long can it last?

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Objective: We present a patient who developed prolonged coma following treatment of ethanol withdrawal with large doses of diazepam and demonstrated prolonged elimination toxicokinetics.
Case report: A 68-year-old man who drank 5-6 alcoholic beverages/day was admitted for an elective transcatheter aortic valve replacement. Two days post-procedure, he developed agitation and was presumptively treated for ethanol withdrawal with diazepam (470 mg IV over 24 hours). He remained comatose for four days prompting a toxicology consult. On day 7 of persistent coma from presumed benzodiazepine excess, flumazenil (0.5 mg) was administered; he opened his eyes for the first time, began speaking, and answering simple questions, but 30 minutes later was comatose again. Flumazenil infusion 0.25 mg/h was trialed with unclear effect. His hospitalization was complicated by gastrointestinal bleeding and mild ischemic stroke deemed noncontributory to his clinical status. The flumazenil infusion was discontinued 1 week later. His evaluation was extensive (brain magnetic resonance imaging and computerised tomography, lumbar puncture, and blood cultures) and unremarkable. On hospital week 4, he became only gradually more awake, and was eventually discharged to a rehabilitation facility on hospital week 6, awake, conversive but still confused. Six weeks later, he was discharged home fully recovered. He remains amnestic to his hospitalization. Serum diazepam and nordiazepam concentrations were determined via liquid-chromatography mass-spectrometry. Concentrations obtained four days after the last dose were: diazepam 963 µg/L (therapeutic: 200-1000 µg/L) and nordiazepam 240 µg/L (therapeutic: 100-1500 µg/L). Elimination kinetics were calculated with apparent half-lives of 294 hours and 797 hours for diazepam and nordiazepam, respectively. Genotyping of CYP3A4 and CYP2C19, the two primary metabolizers of diazepam, demonstrated no abnormalities.
Conclusion: Diazepam demonstrated extremely atypical elimination kinetics despite normal renal and hepatic function. Acute tolerance which is expected after prolonged benzodiazepine

Table 1. Elimination kinetic data in a patient with prolonged coma following treatment of ethanol withdrawal with large doses of diazepam. The last dose of diazepam was 96 hours prior to time = 0.

Diazepam elimination kinetics									
Hours (h)	0	64	133	206	384	540	652	817	1010
Diazepam (d) (µg/L)	963	904	750	828	258	185	169	130	131
ln[d]	**6.870**	**6.807**	**6.620**	**6.719**	**5.553**	**5.220**	**5.130**	**4.868**	**4.875**
Nordiazepam (n) (µg/L)	240	479	538	777	552	457	422	345	402
ln[n]	**5.481**	**6.172**	**6.288**	**6.655**	**6.314**	**6.125**	**6.045**	**5.844**	**5.996**
Derived apparent elimination half-life constants:									
K_e(d) = 0.002357 (R^2=0.8992); $t_{1/2}$ = 294 hours									
K_e(n) = 0.000869 (R^2=0.7795); $t_{1/2}$ = 797 hours									

* Notes: (d) denotes diazepam serum concentration, (n) denotes nordiazepam serum concentration. The numbers in bold are the natural log of serum concentrations. K_e represents the elimination half-life constant. K_e was determined based on semi-ln plot with respect to time. Linear regression was done to determine K_e. K_e(n) was determined based on the above kinetics data with exclusion of the first three serum concentrations due to ongoing absorption.

exposure was not clearly demonstrated. The relationship between his serum concentration and clinical status is unclear at this time.

231. Sarolaner-poisoning in an infant: a case report

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Objective: Sarolaner is an acaricide and insecticide belonging to the isoxazoline family. The primary target of action is functional blockade of ligand-gated chloride channels (GABA-receptors and glutamate-receptors) in the central nervous system of insects and acarines. Sarolaner has a higher functional potency for the blockade of receptors of insects and mites in comparison to receptors of mammals. It does not interact with the known insecticidal binding sites of other insecticides. Sarolaner has been in use for about 4 years. We could not find published cases of human ingestion. In a safety study, dogs received different doses of sarolaner every 28 days for 10 months. Doses given were the normal dose (4 mg/kg body weight), and 3-fold and 5-fold of the maximal treatment dose. The 3-fold dose produced mild neurological symptoms (tremor) and the 5-fold dose convulsions. We report a case of sarolaner poisoning in a child.
Case report: A 2-year-old boy (12 kg), son of a veterinarian, took two chewable tablets of sarolaner 80 mg. After about 50 minutes, the mother observed that the child had an unsteady gait and a tendency to fall and she called the Poisons Information Centre (PIC). Since there were no toxicological data available and symptoms were present, hospitalisation was advised. Two hours after the ingestion the paediatrician diagnosed ataxia, tremor, confusion and hallucinations. Our patient had taken 13.3 mg/kg, which is slightly more than the 3-fold maximal therapeutic dose (related to the dog dose). His symptoms corresponded to those in animal experiments: the child was impaired with startle response, hallucinations and had to be sedated to mitigate the symptoms. Midazolam 1.5 mg was given twice intravenously with an interval of one hour. Thereafter, no further medication was necessary and 10 hours after the ingestion he was only minimally ataxic. Laboratory values were normal except for slightly elevated alanine aminotransferase (ALT) and lactate dehydrogenase (LDH). He was discharged on the following day free of symptoms.
Conclusion: The ingestion of the recently approved veterinary drug sarolaner by children has to be taken seriously, because no data regarding human toxicity are available and severe adverse effects are possible. So far, no specific treatment is known.

232. General characteristics of acute poisonings by hypotensive and antiarrhythmic drugs in Moscow, 2010-2017

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Objective: The ready availability of medications for cardiovascular diseases promotes their uncontrolled use. We studied poisonings by drugs classified by ICD10 in group T46 (agents primarily affecting the cardiovascular system).
Methods: Retrospective analysis of reports from the acute poisoning department of the Moscow Sklifosovsky Research Institute of Emergency Aid, 2010-2017.
Results: Poisonings by hypotensive and antiarrhythmic drugs (including beta-blockers, angiotensin-converting-enzyme (II) inhibitors, calcium channel blockers), caused 5.2-9.4% of acute chemical poisonings each year, which was confirmed by chromatomass spectrometry. During the study period the number of poisonings by alpha-adrenomimetics (clonidine) decreased, but the number of patients with poisoning by beta-blockers and inhibitors of angiotensin-converting-enzyme, especially beta-blockers increased. In 2.7-7.5% of cases there was combined use of cardiovascular drugs with other medications, including phenazepam (bromdihydrochlorphenylbenzodiazepine), doxylamine, phenobarbital, drotaverine, non-steroid anti-inflammatory drugs and antidiabetic drugs. In 40% of patients use of beta-blockers or inhibitors of angiotensin-converting-enzyme was combined with alcohol. Poisoning cases in women ranged from 68-76% each year. Patient age ranged from 15-97 years of which 25-33% of patients each year were elderly. From 13.7-25.7% of patients were younger than 30 years. It was noted that the number of patients younger than 20 years increased from 3.5% in 2012 to 12.3% in 2016. Overall 47-53% of cases involved patients aged 30-59 years. More than 90% of patients used the cardiovascular drugs with suicidal intent. Accidental poisonings, due to mistaken dosage or for self-treatment, increased from 2.1% to 6.7%. Overall 5% of poisonings were criminal (involving clonidine) and on the background of alcohol intoxication. In 2010-2012 and 2017 53.0% of patients were admitted to the intensive care unit and 42.0% in 2014. In the same years the number of patients with mild and moderate poisoning increased from 2.5% to 6.5% and from 41.4% to 46.0%, respectively. In 2012 fatal cases peaked at 8.3% but in the following years this decreased 1.7-1.9-fold. Up to 55% of lethal outcomes occurred in the toxicogenic stage of poisoning and was characterized by cardiovascular shock and/or its combination with cardiotoxic effects. The main reason for a

lethal outcome in the somatogenic stage of poisoning was pneumonia, which occurred in 36-54% of all lethal cases in patients aged 67.3 ± 6.1 years.
Conclusion: Acute poisonings by hypotensive and antiarrhythmic drugs is a medical and social problem in connection with the increasing prevalence of these drugs, especially in young and middle-aged adults. Overdose of these drugs is associated with a high lethality.

233. Acute toxicity profile of levomepromazine in overdose: a consecutive case series

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Objective: Levomepromazine (methotrimeprazine) is a phenothiazine neuroleptic drug that acts as an antagonist at histamine type 1, muscarinic-cholinergic, dopaminergic-2, alpha-1 adrenoceptor and 5HT-2 receptors. It is approved in adults, and not recommended for pediatric use. The oral dosage varies from 25-200 mg daily, depending on individual response. Levomepromazine is widely used, especially in terminally ill patients. However, information on the clinical features of levomepromazine poisoning is lacking. The aim of this study was to investigate the demographics and clinical features of acute levomepromazine overdose.
Methods: A retrospective review of single-substance acute oral overdose with levomepromazine in adults and children (< 16 years), reported to our poison centre 1997-2018.
Results: Overall 189 patients (median age 31, range 0.8-88 years) were included with 133 females (70%), 52 males (28%) and 4 unknown. There were 167 adults (88%) and 22 children (12%) with median age 13.8 years (range 0.8-15.8 years). No symptoms developed in 16 adults (10% of adults) and 2 children (9% of children). Mild symptoms were seen in 111 adults (66%) and 18 children (78%). Moderate symptoms occurred in 33 adults (20%) and 2 children (9%), and 7 adults (4%) had severe symptoms. There were no fatalities. Effects predominantly involved the central nervous system, with somnolence reported in two-thirds of the patients. Tachycardia and hypotension were also common findings. Furthermore, severe cardiovascular and respiratory symptoms were reported (Table 1). In 6 of 7 patients severe symptoms occurred after intentional ingestion. The majority of patients (23/28) with moderate symptoms ingested >750 mg (median 1000 mg), 5/7 patients with severe symptoms ingested ≥1250 mg (median 3250 mg) of levomepromazine.
Conclusion: Levomepromazine displays an acute toxicity profile similar to other phenothiazine neuroleptics [1].

Table 1. Signs and symptoms and their severity (Poisoning Severity Score) in patients with acute levopromazine overdose (n = 189). Overall the median reported levomepromazine dose (n = 163) was 0.75 g (range 0.01-9.5 g, mean 1.2 g).

		Severity		
	Symptom / Sign	Mild n (%)	Moderate n (%)	Severe n (%)
Central nervous system	Somnolence	122 (65%)	0	0
	Coma (moderate: GCS 8-9; severe: GCS ≤7)	0	7 (4%)	6 (3%)
	Drowsiness	5 (3%)	0	0
	Miosis	16 (8%)	0	0
	Dysarthria	13 (7%)	0	0
	Dry mouth	12 (6%)	0	0
	Dystonic reaction (mild: focal dyskinesia; moderate: multifocal dyskinesia, glossopharyngeal spasms; severe: opisthotonus)	7 (4%)	2 (1%)	1 (0.5%)
	Agitation	6 (3%)	4 (2%)	0
	Confusional state	0	6 (3%)	0
	Disorientation	0	2 (1%)	0
	Vertigo	5 (3%)	0	0
	Tremor	5 (3%)	0	0
	Gait disturbance	4 (2%)	0	0
	Seizures (moderate: single convulsive episode)	0	1 (0.5%)	0
	Hallucinations	0	1 (0.5%)	0
Cardiovascular system	Tachycardia (adults, mild: 100-139 beats/min; adults, moderate 140-179 beats/min; children, (< 2 years) moderate: > 205 beats/min)	25 (13%)	1 (0.5%)	0
	Hypotension/orthostasis (adults, moderate: 55-79 mmHg, children, moderate: 40-49 mmHg)	17 (9%)	2 (1%)	0
	QT-prolongation (children (1-15 y), mild: QTc 440-500 ms; adults, males, mild: 430-500 ms; adults, females, mild: 450-500 ms; adults moderate: > 500 ms)	13 (7%)	6 (3%)	0
	Bradycardia (adults, moderate 40-50 beats/min; children moderate: 60-80 beats/min)	3 (2%)	3 (2%)	0
	Other ECG disturbances (mild: partial bundle branch block, supraventricular extrasystoles; moderate: AV-block I, QRS >100 ms, severe: ventricular fibrillation)	4 (2%)	3 (2%)	1 (0.5%)
Respiratory system	Respiratory depression/apnoea	5 (1%)	0	1 (0.5%)
Various	Gastrointestinal symptoms (mild: nausea, mild vomiting, epigastric pain)	12 (6%)	0	0
	Electrolyte disturbances (mild: potassium 3.0-3.4 mmol/L)	8 (4%)	0	0
	Mydriasis	2 (1%)	0	0
	Elevated transaminases	3 (2%)	0	0

Reference

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234. Be(a)ware of the fentanyl patch: unusual accidental cases of fentanyl intoxication

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Objective: The misuse of fentanyl from patches is well known. Fentanyl is scraped from the patch and smoked or inhaled. We draw attention to an unusual route of intoxication with a fentanyl patch.
Case reports: An 87-year old woman in a nursing home was found in her room at 11:45, unconscious and snoring. She was brought to the emergency department, where she was evaluated for possible causes such as a cerebral event or metabolic dysregulation. None of these could be demonstrated and she was sent back to her nursing home. At that time she only reacted to strong painful stimuli. At 18:00 a nurse took her dental prosthesis out. Around 21:15 a slimy fentanyl patch was discovered in her mouth; this had been applied to the skin three days previously. At 23:00 she was fully awake, but her respiratory rate was still low at 12 per minute. In another case, another woman, 84-years-old with dementia, was found unconscious in her nursing home. Later her caregivers noticed a fentanyl patch sticking under her dental prosthesis. She did not have her fentanyl patch on her back anymore so it was likely that she had changed the position of this patch herself.
Conclusion: The unintentional intoxication described in these cases is rare and it took some time before the hidden patches were discovered. There are a few interesting aspects. Fentanyl patches removed from the skin after three days can still contain a large amount of fentanyl: 4.46-8.45 mg (45-85%) from 10 mg patches [1]. Secondly, fentanyl can be absorbed well through oral mucosa; a characteristic of rapid onset opioids (ROOs). Different fentanyl ROOs show different pharmacokinetic patterns, yet all show good transmucosal absorption (with a C_{max} of 0.7-0.95 ng/mL with equipotent doses) and sustained concentrations when there is a continuous supply [2]. These accidental cases describe the risk from fentanyl patches, which can be hidden in unsuspected places and following transmucosal absorption of fentanyl, lead to intoxication. Caregivers and healthcare professionals need to be aware of this route in cases of an opioid intoxication with no known intake.

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235. Calls to the Finnish Poison Information Centre related to drug poisoning in older people

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Objective: To investigate the reasons and drugs most frequently involved in calls made to the Finnish Poison Information Centre (FPIC) concerning elderly citizens.
Methods: Research data was collected from the database of the FPIC. All calls received between the years 2012 and 2016 concerning people aged 65 years and older were included.
Results: The total number of calls included in the study was 8847. More than half (n = 4857, 54.9%) of the calls were drug-related and 9.4% (n = 836) of the calls concerned medication errors made by healthcare professionals. The most common groups of drugs represented in the calls were drugs affecting the cardiovascular or nervous system. Among the elderly, the most common reasons for calling the FPIC were errors in doses (20.9%), dosage (13.5%) or consuming drugs of other people (49.4%).
Conclusion: Errors in drug therapy are a reason for a significant number of calls concerning elderly people. Drugs affecting the cardiovascular and nervous system were mostly represented in these calls and likely reflect their frequent use among the elderly. In addition, drug therapy errors made by healthcare professionals cause numerous poisoning cases, many of which could be avoided.

236. Preliminary experience with plasmapheresis instead of molecular adsorbent recirculating system as liver support for paracetamol-induced hepatic failure

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Objective: We aimed to analyze retrospectively the indication and use of plasmapheresis as liver support in intensive care unit (ICU) patients admitted for paracetamol-induced hepatic failure.
Methods: A comparison is proposed between paracetamol poisoned patients who were treated with the molecular adsorbent recirculating system (MARS™) that was previously in use in the ICU, patients treated with plasmapheresis, and patients who received standard supportive care.
Results: Over the period 2007-2019, 104 paracetamol-poisoned patients were referred to the ICU with ALT >1000 IU/L and a delay for first administration of N-acetylcysteine >12 hours. The etiology was either suicidal ingestion or accidental poisoning with supra-therapeutic doses. Modified King's College Criteria were used for identification of patients requiring transplantation. The patients were classified into 3 groups: standard care (SC) (n = 72), MARS™ (M) (n = 14), or plasmapheresis (P) (n = 18) (starting from 2015). There was no difference in age or gender. Both M and P groups had higher admission Sequential Organ

Failure Assessment (SOFA) scores ($p < 0.001$). As expected, the following variables were higher in the M and P groups: need for renal replacement therapy ($p < 0.001$), shock ($p < 0.001$), need for mechanical ventilation ($p < 0.001$), infection rate ($p = 0.044$), and criteria for liver transplantation ($p < 0.001$). Regarding King's College Criteria, they were met for 3 patients in the SC group (4%), 14 (100%) in the M group, and 12 (71%) in the P group. Patients effectively transplanted were 6 (43%) in the M group and 4 (24%) in the P group, versus 0 in the SC group. Fatalities were 4 (29%) in the M group, and 6 (33%) in the P group, versus 4 (6%) in the SC group. Among biological criteria (arterial pH, lactate, bilirubin, factor V, INR, ammonia), only maximal ammonia concentration was lower in the P group in comparison with the M group ($p < 0.001$).
Conclusion: Retrospectively, we found that the most severe patients were adequately identified to receive either MARS™ or plasmapheresis as liver support for paracetamol-induced hepatic failure. The populations treated with M or P were rather similar, even if the use of plasmapheresis was probably more liberal in the ICU as the technique is available and reimbursed, while M is not [1].

Reference

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237. Acute poisoning with antihypertensive drugs: a retrospective study

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Objective: The aim of this study was to analyse the characteristics of acute poisoning cases admitted to the Toxicology Clinic, UMHATEM "N.I.Pirogov".
Methods: A retrospective review of all patients poisoned with antihypertensive drugs, treated in our Clinic between January and August 2018 was performed. Demographic data, presenting syndromes, previous illness, laboratory tests, ECG abnormalities, were obtained retrospectively from the patients' charts. The cases were evaluated with respect to clinical course, therapy and outcome.
Results: A total 26 patients with acute exogenous intoxication with antihypertensive medicines were treated in the Toxicology Clinic, Department for Adults over the study period. Antihypertensive medicines included angiotensin converting enzyme (ACE) inhibitors, beta-blockers, calcium channel antagonists, vasodilators, and other antihypertensive drugs. Patients were aged between 20 and 86 years and the majority ($n = 18$, 69.2%) were over the age of 40 years. Most of them were female ($n = 18$, 69.2%; male $n = 8$, 30.8%). In 15 cases (57.7%) only one antihypertensive drug was taken and in 11 cases (42.3%) more than one medicinal drug was taken. The common co-ingestants included other antihypertensive drugs, benzodiazepines, antidepressants, neuroleptics, and ethanol. Clonidine was involved in the majority of the cases ($n = 16$, 61.5%). Ingestion was intentional in 23 cases (88.5%). The main causes of suicide attempts were various kinds of depression as well as cognitive disorders. The severity of poisonings varied from moderate to extremely severe. In 3 patients poisoning occurred with the signs of exotoxic shock. Cardiotoxic syndrome (hypotension, bradycardia) was present in all cases, and cerebral toxic syndrome was noted in 7 cases. There were no deaths. Management in all cases was supportive with the main treatment modality being intravenous fluids, gastric lavage, activated charcoal, oxygen, crystalloid resuscitation, atropine, vasoactive agents (adrenaline, noradrenaline, dopamine), respiratory support, and symptomatic treatment.
Conclusion: Acute self-poisoning with antihypertensive medicines has become an important cause of admission to our toxicology department. The number of cases has increased in the last few years. These drugs are responsible for major morbidities, as more people are treated for hypertension.

238. Rectal overdose of paracetamol

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Objective: Clinically relevant overdoses of paracetamol with suppositories via the rectal route are rare and, to our knowledge, not described previously in the literature. Theoretically toxicity might be reduced by rectal administration as there is no first pass metabolism after absorption in the lower part of the rectum, however, the upper part of the rectum is connected to the portal vein and there are abundant venous anastomoses with the lower part. Management of a rectal overdose may need different considerations compared to that of an ordinary overdose of paracetamol. Rectal doses of paracetamol have a prolonged absorption phase and a delayed peak of the serum paracetamol-concentration compared to oral doses [1]. This should limit the ability to use the paracetamol nomogram. Here, a massive (50 g) rectal overdose of paracetamol with signs of delayed absorption is presented.
Case report: A 54-year-old man with a history of psychiatric disease administered 50 g (100 × 500 mg suppositories) over 2.5 hours as an attempt to reduce anxiety. Seven hours after the last administration he presented at the hospital. On arrival he was anxious and had nausea but was otherwise fit. The blood paracetamol concentration was 1094 µmol/L (165 µg/mL). Eleven hours after the overdose the concentration was 1292 µmol/L (195 µg/mL). At nineteen hours it was 149 µmol/L (22.5 µg/mL). He was treated with an enema and an N-acetylcysteine infusion was started eleven hours after the overdose. N-Acetylcysteine was administered as a bolus dose of 150 mg/kg for 15 minutes followed by an infusion of 12.5 mg/kg/h (increased dose due to the high paracetamol concentrations) for 25 hours (slightly prolonged infusion since treatment was started eleven hours after the overdose). The transaminases were normal throughout the hospital course and he was discharged two days after the overdose.
Conclusion: This case illustrates that rectal overdoses of paracetamol may be clinically significant. The fact that the paracetamol concentration continued to increase after 7 hours from the overdose implies that absorption may be delayed and prolonged and that the treatment nomogram is probably not applicable. In rectal overdoses blood paracetamol concentrations should be followed until they have peaked and start to decline.

Reference

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239. Torsade de pointes following repeated massive loperamide ingestion

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Objective: Loperamide is a mu-opioid receptor agonist with poor systemic bioavailability after normal dosing. However, after massive doses bioavailability increases, partly due to overwhelmed P-glycoprotein counter transport capability, and central mu-opioid symptoms arise. This pharmacokinetic loophole has led to a noticeable increase in loperamide poisoning in Sweden in the last decade with 21 cases appearing in the Poison Center records in 2018, up from barely detectable levels a decade earlier. Loperamide deaths have also started to appear in forensic records in recent years, with 5-10 fatalities in Sweden annually. The high doses of loperamide needed to induce central opioid effects lead to complications from off target effects on the heart, which has been described in several recent publications [1–3]. With this case report we add to this literature with a case of syncope and prolonged QTc intervals and bursts of torsade de pointes (TdP).
Case report: A 42-year-old woman fainted in her home and was brought to the emergency department. On arrival she was awake, with an ECG showing sinus rhythm with multiple ectopic beats, a widened QRS of 142 ms, QTc of 465 ms, and a heart rate of 80/minute. At the cardiology ward she experienced 2 episodes of TdP. The first episode self-terminated, while the second was successfully defibrillated to sinus rhythm. A prophylactic temporary pacemaker was put in place, and potassium and calcium were substituted to the upper level of the normal interval and she received a magnesium infusion. On the second day she revealed that during the previous year she had been taking 48-160 tablets of loperamide daily (i.e. 6-20 times higher than the recommended maximum daily dose). On day 4 and 6 of her hospitalization, recurrent episodes of TdP occurred that were terminated by over-drive pacing. On day 9 the pacemaker was removed. The patient was discharged on day 11 with a normal ECG.
Conclusion: Our poison centre has recently been involved in two additional cases of repeated overdoses of loperamide, with prolonged QTc time and episodes of TdP. Loperamide should be considered a high-risk pharmaceutical regarding development of TdP.

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240. The risks of fentanyl patches in outpatient pain therapy: a 20-year retrospective pharmacovigilance analysis from northern Germany

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Objective: Since the 1990s fentanyl transdermal therapeutic systems (TTS) such as fentanyl patches are increasingly used in the pain management of outpatients. Like other opioids fentanyl has a high potential for abuse and a narrow therapeutic range, hence the risk of accidental or abusive poisoning is high. We reviewed enquiries about fentanyl patches reported to the GIZ-Nord Poisons Centre.
Methods: All inquiries about fentanyl patches for the period 1998-2018 to the GIZ-Nord Poisons Centre were identified. The circumstance, symptoms, severity, and ToxIndex were analyzed.
Results: Over the 20 year period the poisons centre registered a more than tenfold increase of incidents with fentanyl patches. Overall 159 cases were identified. The majority of patients were adults and only 3 cases (2%) involved children. The vast majority of intoxications occurred at home, followed by nursing homes. The conditions of exposure were: accidental (28%), abuse (19%), suicidal (17%), not documented (n.d.) (16%), iatrogenic (10%), adverse drug reaction (9%), and confusion of pharmaceuticals (1%). Severity was classified according to the Poisoning Severity Score (46% minor, 26% moderate, 13% severe, 4% not documented and 9% no symptoms). Two fatalities were registered (l1.3%). This figure is likely due to the fact that in most pre-hospital deaths, poison centres are rarely involved. The main symptoms were central nervous system depression (55%), respiratory depression (20%), and nausea or vomiting (14%). The ToxIndex is defined as the sum of all cases classified as lethal, severe, or moderate in relation to the number of all cases. This index for intoxication with fentanyl patches was very high at 40%.
Conclusion: The use of fentanyl-patches for pain therapy has increased over the last 20 years. During this period the GIZ-Nord Poisons Centre registered increasing inquiries with these therapeutics. The calculated ToxIndex of these data indicates the high risk associated with this form of fentanyl. European poisons centres play a key role in pharmacovigilance. They should monitor incidents with opioid-TTS to support responsible agencies in undertaking a risk analysis for these therapies.

241. Angiotensin axis antagonists increase the severity of dihydropyridine poisoning

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Objective: Angiotensin axis antagonist drugs are typically benign in overdose [1], but are often taken with other antihypertensive agents. Our aim was to investigate the effect of combined angiotensin axis antagonist drug and dihydropyridine calcium channel blocker (DHP CCB) overdose versus dihydropyridine overdose alone.

Table 1. Comparison of demographics and outcomes of patients with angiotensin-converting-enzyme inhibitor (ACEI) overdose with and without co-ingestion of dihydropyridine calcium channel blocker (DHP CCB) [medians (IQR) or n (%)].

Parameter	DHP CCB with ACEI/ARB (n = 68)	DHP CCB without ACEI/ARB (n = 32)	P-value
Median age (years)	54 (IQR 45-61)	51.5 (IQR 35-67)	0.684
Female	39 (57%)	18 (56%)	0.917
Ingested dose (DDDs of DHP CCB)	22 (IQR 10-40)	13 (IQR 7-30)	0.058
Lowest MAP (mmHg)	62 (IQR 56-68)	75 (IQR 69-80)	<0.0001
Lowest heart rate (bpm)	70 (IQR 60-78)	80 (IQR 71-83)	0.001
Received IV fluids	63 (93%)	22 (69%)	0.002
Received antidote or inotropes	24 (35%)	5 (16%)	0.043
ICU admission	18 (26%)	6 (19%)	0.399
Length of stay (days)	1.3 (IQR 0.7-2.2)	0.9 (IQR 0.5-1.6)	0.101

Defined Daily Doses (DDD): amlodipine 5 mg, felodipine 5 mg, lercanidipine 10 mg, nifedipine 30 mg.

Methods: This is a retrospective study of patients reported to the New South Wales Poisons Information Centre (NSW PIC) and three toxicology units (January 2016 to June 2019). Patients aged ≥15 years who took an overdose of dihydropyridines (amlodipine, felodipine, lercanidipine, nifedipine) were included. Patients who took a concurrent overdose of non-dihydropyridine CCB, alpha-blocker or beta-blocker were excluded. We recorded patient demographics, drugs ingested, size of overdose (in Defined Daily Doses (DDDs), vital signs, treatment and outcome. Multivariable regression was used to identify predictors for hypotension.
Results: We identified 100 patients with dihydropyridine overdose meeting our inclusion criteria; 68 of these also ingested angiotensin axis antagonist drugs. The mixed ingestion group had a lower mean arterial pressure (MAP) ($p < 0.0001$), and required more interventions, such as inotropes and/or calcium salts (OR: 2.3, 95%CI: 0.7-7.4) and intravenous fluids (OR: 4.9, 95% CI: 1.5-16.3) (Table 1). Multivariable regression showed the main risk factors for lowest MAP were age ($p = 0.03$), dose ingested ($p < 0.001$) and mixed dihydropyridine overdose ($p = 0.002$). There were no fatalities.
Conclusion: Combined dihydropyridine and angiotensin axis antagonist overdose was common and caused more hypotension and required more haemodynamic support than dihydropyridine overdose alone.

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242. A case series of flecainide poisoning

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Table 1. A case series of flecainide poisoning.

Parameter	Flecainide and $NaHCO_3$ (range) n = 5	Flecainide and no $NaHCO_3$ (range) n = 2
Median age (years)	49 (17-74)	73
Female	60%	100%
Median dose (g)	2.0 (1.5-6.0)	0.8 (0.3-1.3)
Median minimum heart rate during admission	59 (51-65)	76 (74-77)
Median minimum mean arterial pressure (MAP) during admission (mmHg)	56 (44-71)	73 (52-95)
Median minimum Glasgow Coma Score (GCS) during admission	3 (3-14)	–
Intubated	100%	0%
Median maximum QRS during admission (ms)	190 (129-240)	102 (97-107)
Number of patients with arrhythmia	2	0
Median serum pH at admission	7.36 (7.29-7.54)	7.44
Median increase in serum pH during admission	0.15 (0.00-0.21)	0.00
Length of stay (days)	8.3 (0-19)	0.2

Objective: Flecainide is a class 1C antiarrhythmic agent and a potassium channel blocker. Flecainide poisoning is relatively rare, but is highly toxic with a reported mortality rate of approximately 10% [1]. There is evidence that increases in extracellular sodium concentration can reverse the sodium channel blocking effect. However, alkalaemia can induce hypokalaemia, exacerbating QT prolongation. We describe a case series of flecainide poisoning and the changes in biochemical profile following treatment.
Methods: A retrospective review of patients with flecainide poisoning from 2 toxicology units and the New South Wales Poisons Information Centre (January 2013 – June 2019). A pre-formatted Redcap database was used to record patient demographics, dose ingested, signs and symptoms of toxicity, biochemical profile, ECG, treatment and outcome.
Results: There were 7 patients with flecainide toxicity (Table 1). Five patients received sodium bicarbonate ($NaHCO_3$) while two patients did not. Of the 5 patients who received bicarbonate therapy, median dose given was 300 mmol (range: 100-700). The median increase of sodium and bicarbonate ions were 5 (range: 0-6) and 2.2 mmol/L (range: 0-11.3) respectively, while pCO_2 and potassium were reduced by 7 mmHg (range: 4-10) and 0.8 mmol/L (range: 0-1.6), respectively. The median increase in serum pH was 0.15 (range: 7.29-7.54). The QRS decreased [2] by >30 ms or narrowed to <110 ms at a median time of 2.9 hours (range 2.7-3.8) with hyperventilation and bicarbonate therapy. There was no fatality.
Conclusion: Alkalinisation with bicarbonate and hyperventilation appeared to be effective in managing flecainide poisoning.

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243. Effect of serum alkalinisation on QRS narrowing in tricyclic antidepressant poisoning

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Objective: Sodium bicarbonate ($NaHCO_3$) is widely accepted as a treatment to achieve alkalinisation in tricyclic antidepressant (TCA) poisoning but evidence is lacking [1]. We quantify the effects of sodium bicarbonate ($NaHCO_3$) and hyperventilation on the rate of QRS narrowing in TCA poisoning.
Methods: This is a retrospective review of patients who had ≥10 mg/kg TCA ingestion or symptoms of TCA poisoning (January 2013-June 2019). Patients were included from 2 toxicology units and the New South Wales Poisons Information Centre. The time taken for the QRS to narrow was measured from the earliest time when the QRS was widened (defined as >110 ms) to the earliest time when the QRS decreased by >30 ms or narrowed to <100 ms. The patients were divided into 2 groups: $NaHCO_3$ AND hyperventilation dual therapy group or supportive care ± hyperventilation or $NaHCO_3$ treatment group.
Results: Of 160 patients who had ≥10 mg/kg or symptoms of TCA poisoning, 86 patients (54%) received $NaHCO_3$ treatment. Median dose of $NaHCO_3$ was 200 mmol (IQR: 100-300). Of 84 patients who had QRS >110 ms, 51 patients received $NaHCO_3$ and hyperventilation while 33 patients received either $NaHCO_3$ (n = 7), hyperventilation (n = 11) or supportive care alone (n = 15). There were 28 patients (33%) who subsequently had QRS narrowing, 23/51 receiving dual therapy and 5/33 receiving other treatment. The median time to narrow QRS duration was 2.8 h (IQR: 1.8-5.7 h) after dual therapy and 7.1 h (IQR: 5.4-9.8 h) (p = 0.008) for the other patients. Cox regression analysis showed that patients were 3 times more likely to have QRS narrowing if they received dual therapy when compared with other treatment strategies (OR: 3.1, 95% CI: 1.2-8.2, p = 0.02).
Conclusion: Sodium bicarbonate and hyperventilation combination therapy was more effective in narrowing the QRS when compared with supportive treatment alone, or in addition to either $NaHCO_3$, or hyperventilation treatment.

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244. Optimal way to achieve serum alkalinisation in tricyclic antidepressant overdose

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Objective: It is widely accepted to use sodium bicarbonate ($NaHCO_3$) therapy to achieve alkalinisation in managing tricyclic antidepressant (TCA) poisoning, but it is not clear what the optimal dose should be. We determine the optimal method to achieve serum alkalinisation in patients with TCA poisoning and develop and evaluate a model to predict the dosage of sodium bicarbonate to achieve serum alkalinisation.
Methods: This is a retrospective review of patients who had TCA overdoses from 2 toxicology units and the New South Wales Poisons Information Centre (January 2013–June 2019). We compared the different treatments to achieve serum alkalinisation. We developed a formula based on the Henderson-Hasselbalch equation to predict the change in pH following $NaHCO_3$ therapy and/or hyperventilation. We measured the agreement and limits of agreement to analyse the accuracy of the pH model with patient data. This equation was then utilised to predict the quantity of $NaHCO_3$ therapy required coupled with hyperventilation aiming for a pCO_2 close to 30 mmHg to generate a nomogram.

$$pH_{after\ treatment} = 6.1 + \log\left(\frac{[serum\ HCO_3^-]_{after\ treatment}}{0.03 \times PCO2_{after\ treatment}}\right)$$

$$[serum\ HCO_3^-]_{after\ treatment} = [serum\ HCO_3^-]_{before\ NaHCO_3} + \frac{NaHCO_3}{40} + 0.2 \times \Delta PCO2$$

Results: There were 74 patients who had $NaHCO_3$ and hyperventilation treatment, while 86 patients had either bicarbonate (n = 12), hyperventilation (n = 32) or supportive care therapy (n = 42). In the $NaHCO_3$ treatment group, the median dose of bicarbonate was 200 mmol (range 50-1000), with a median increase of sodium and bicarbonate of 2 and 1 mmol/L, respectively within 12 hours of admission. The median pH achieved following $NaHCO_3$ alone and $NaHCO_3$ AND hyperventilation treatment was 7.43 (IQR: 7.39-7.46) and 7.5 (IQR: 7.43-7.56), respectively. Patients who had hyperventilation and bicarbonate therapy had the greatest increase in pH (median: 0.12, IQR:0.04-0.18) when compared with single or supportive therapy only (median: 0; IQR:0-0.11) (p < 0.0001). There were 99 patients who had an increase in serum pH recorded and the interclass correlation coefficient to the predicted increases in serum pH was 0.84 (95%CI: 0.77-0.9). A decrease of pCO_2 by 10 mmHg increased pH by 0.05 while the administration of 100 mmol sodium bicarbonate increased pH by 0.05 (ICC: 0.8, 95%CI: 0.7-0.9). We created a nomogram to predict the dose of sodium bicarbonate needed to achieve a serum pH 7.5, if the pCO_2 is decreased to 30 mmHg with hyperventilation.
Conclusion: Alkalaemia is best achieved with hyperventilation and $NaHCO_3$ therapy in TCA poisoning. It is feasible to predict the optimal dose of bicarbonate therapy that coupled with hyperventilation (pCO_2 30 mmHg) will reliably achieve an optimal pH around 7.5.

245. A 10-year review of enquiries to the UK National Poisons Information Service involving high-dose insulin (HDI)

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Objective: To review enquiries to the UK National Poisons Information Service (NPIS) involving high-dose insulin (HDI).
Methods: A retrospective analysis was undertaken between 1 January 2009 and 31 December 2018 for enquiries relating to HDI administration.
Results: There were 954 relevant enquiries involving 763 patients of whom 340 received HDI, 125 did not and it was unknown if HDI was given in 298 patients. The number of patients given HDI ranged from 10 in 2009 to a peak of 58 in 2017. Ten patients given HDI were aged 16 years or less. The mean age was 48 years (range 12-89 years). Polypharmacy ingestions were involved in 81% of cases (n = 274) most often including calcium channel blockers (CCB) n = 196 and beta-blockers n = 129. Single drugs were taken in 65 cases: CCB n = 34, beta-blocker n = 24, tilmicosin n = 1, tricyclic antidepressant n = 1, and other drugs n = 5. In one case the substance was unknown. Conventional inotropes had already been given to 70% (n = 239) of patients prior to being treated with HDI and 61% (n = 207) had already been given glucagon (60% of these cases involved a beta-blocker). Hypoglycaemia was reported in 10% of enquiries (n = 34) and hypokalaemia in 4.7% (n = 16). Advice was sought about the discontinuation of the insulin infusion in 16% of all patients known to have been treated with HDI. Maximum administered insulin infusion doses documented were <3 unit/kg/h in 121/340 cases, 4-9 unit/kg/h in 30 cases, 10 unit/kg/h in 31 cases and >10 unit/kg/h in 6 cases. In 152 cases the infusion doses were unknown. The largest insulin infusion dose was 20 unit/kg/h which was given to 4 patients who had all taken mixed overdoses including amlodipine (n = 3), bisoprolol (n = 1) and flecainide (n = 1). Hypoglycaemia and hypokalaemia were not reported in any of these 6 patients. The outcome of the 6 patients given >10 unit/kg/h was complete recovery (n = 2), death (n = 2) and the outcome in the remaining 2 patients is unknown. Outcome in the 340 cases where HDI was given were complete recovery (n = 124), sequelae (n = 12, mainly hypoxic brain injury and renal impairment), death (n = 86) and ongoing features at the time follow-up was discontinued (n = 55). The outcome was unknown in the remaining 63 cases.
Conclusion: Enquiries regarding the discussion of HDI have increased over the last 10 years. The majority of enquiries where HDI is given involve polypharmacy overdoses of CCB and beta-blockers. Doses of >10 unit/kg/h were used in 6 of 340 cases.

246. An uncommon cause of high-anion gap metabolic acidosis after repeated supratherapeutic paracetamol ingestion

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Objective: High-anion gap metabolic acidosis (HAGMA) most commonly results from excess urea, lactate, ketones and exposure to toxins such as salicylate and toxic alcohols. Accumulation of pyroglutamic acid (PGA) is a rare cause of HAGMA. The exact incidence of HAGMA caused by PGA accumulation is unknown. A recent prospective study reported that high urine PGA concentrations were associated with 10% of patients with HAGMA. PGA is processed by the glutamate-glutathione cycle. The commonest cause of PGA accumulation is glutathione depletion. This causes the loss of negative feedback on gamma-glutamylcysteine (PGA precursor) production. Other causes include malnutrition, alcoholism, liver failure and sepsis. Though rare, deficiency of either glutathione synthetase causing gamma-glutamylcysteine (PGA precursor) accumulation or 5-oxoprolinase resulting in reduced PGA metabolism, also cause PGA accumulation. We describe a case of confirmed PGA accumulation after repeated supratherapeutic paracetamol use.
Case report: A 32-year-old female presented with ongoing pain from shingles despite having taken 96 x 665 mg modified-release paracetamol caplets over the preceding two days. Two years prior, she suffered a gastric ulcer perforation following excessive ibuprofen use for dysmenorrhea. She subsequently ceased using NSAIDs and substituted these with regular use of four modified-release paracetamol tablets every 3-4 hours. On presentation vital signs were normal except a respiratory rate of 24/min. Venous blood gas showed pH 7.04, bicarbonate 5.0 mmol/L, pCO_2 19 mmHg, lactate 1.4 mmol/L, sodium 150 mmol/L, chloride 117 mmol/L and anion gap 28, indicating a partially compensated HAGMA. Serum ketones were 2.8 mmol/L, salicylate undetected and normal osmolar gap. Serum paracetamol was 312 µmol/L, 2.5 hours after the last dose. Liver function, INR and creatinine were normal. PGA accumulation from chronic paracetamol misuse and glutathione depletion was suspected. Acetylcysteine was infused for 20 hours to replenish glutathione. Other treatment included intravenous crystalloids and sodium bicarbonate infusion. Metabolic acidosis resolved completely over 36 hours. Serum ALT and INR remained normal. She was discharged after three days. A qualitative urine assay was positive for PGA (5-oxoproline).
Conclusion: In this case, chronic excessive paracetamol use compounded by a staggered paracetamol overdose most likely lead to glutathione depletion and PGA accumulation. Treatment included ceasing paracetamol and glutathione replenishment with acetylcysteine therapy. In the absence of enzyme deficiencies, HAGMA from PGA accumulation is unlikely to recur once glutathione is replenished. PGA accumulation should be considered in the differential diagnosis of unexplained HAGMA, especially with a history of excessive supratherapeutic paracetamol use.

247. Using "symptom search" to resolve an unusual case of poisoning reported to the UK National Poisons Information Service (NPIS)

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Objective: "Symptom search" is a function on the UK online poisons information database, TOXBASE® to assist users in the context of an unknown poisoning. We present an unusual case with unknown aetiology reported to the UK National Poisons Information Service (NPIS) in which the use of "symptom search" proved diagnostically valuable.
Case report: A 62-year-old male with a background of chronic obstructive pulmonary disease (COPD) presented to hospital complaining of epigastric pain and shortness of breath. He denied taking any overdose. On examination he was dyspnoeic but otherwise well. His arterial blood gas demonstrated a respiratory acidosis (pH 7.30, pCO_2 7.0 kPa) prompting treatment for an acute exacerbation of COPD. Twelve hours post-admission he experienced a brief episode of asystole, accompanied by a transient fall in systolic blood pressure to 50 mmHg. He became drowsy and increasingly acidotic (pH 7.16, lactate 8.9 mmol/L). Ischaemic bowel was suspected, and he was intubated and ventilated in the intensive care unit. At 18 hours post-admission, his pH fell to 6.97 (lactate 14.4 mmol/L) and he was noted to have an increased alanine aminotransferase activity of 815 IU/L (normal <40). CT abdomen excluded ischaemic bowel. The NPIS gave advice on potential toxicants including toxic alcohols and paracetamol. At 22 hours post-admission the patient was extremely bradycardic (30 bpm) and hypocalcaemic (ionised calcium 0.7 mmol/L). He developed further intermittent periods of asystole prompting administration of IV isoprenaline, calcium gluconate and external pacing. Utilisation of the TOXBASE® "symptom search" function with terms "asystole", "metabolic acidosis "and "hepatotoxicity "suggested poisoning due to calcium channel blockers. The enquirer was recontacted and further investigation revealed for the first time that the patient was on a regular prescription of verapamil. Verapamil overdose was suspected. High-dose insulin (1 unit/kg/h) was initiated and the blood pressure improved. Through semi-quantitative analysis, "high" quantities of verapamil were detected in the patient's plasma by ultra-performance liquid chromatography with exact mass time of flight spectrometry (Waters ACQUITY UPLC system, Xevo G2 QTof detector). On follow-up 6 days later, the patient had regained a normal haemodynamic and acid/base status, but sustained hypoxic brain injury with reasonable neurological function.
Conclusion: "Symptom search" may be a valuable diagnostic aid in the case of unknown poisoning.

248. Favorable toxicity profile of escitalopram in acute overdose in adults

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Objective: Escitalopram is the active S-enantiomer of citalopram and an inhibitor of serotonin reuptake, commonly prescribed for depression and anxiety disorders. Recommended daily oral doses range from 10-20 mg/day. The aim of this study was to investigate demographic and clinical features of acute overdoses with escitalopram.
Methods: A retrospective study of acute, single agent oral overdose with escitalopram in adults reported to our national poisons information centre between 2007 and 2018. We included patients aged ≥16 years with ingestion of a defined dose, documented follow-up and high causality between drug exposure and symptoms. Severity of symptoms was assessed according to the Poisoning Severity Score.
Results: Overall, 154 patients met the inclusion criteria (median age 26, range 16-92 years) and consisted of 115 females (75%) and 39 males (25%). The circumstances of the exposure were intentional (n = 140, 91%), accidental (n = 13, 8%) and therapeutic error (n = 1, 1%). Ingested dose ranged from 25 to 2040 mg (median 200 mg). Asymptomatic patients (n = 28; 18%; median age 22 years range 16-92 years) ingested doses between 25 and 980 mg (median 150 mg). Three patients received single dose activated charcoal (SDAC). For 23 patients (82%) ECG information was available and showed normal findings. A total of 107 patients (69%) (median age 27 years, range 16-85 years) showed mild symptoms with tachycardia (n = 32; 30%), somnolence (n = 29; 27%) and vomiting (n = 27; 25%) as predominant clinical features after an ingested dose between 30 and 2040 mg (median dose 200 mg). In 83 cases (78%) ECG information was available; abnormal ECG findings were QTc prolongation of maximum 500 ms in 21 patients (25%). Fourteen patients received SDAC. Nineteen patients (12%) (median age 27 years, range 17-73 years) had moderate symptoms after ingesting 50 to 1520 mg (median 280 mg) including agitation and confusion (n = 11; 58%), stupor (n = 2; 11%), single episode of seizure (n = 1; 5%), QTc prolongation >500 ms (n = 7; 36%), urinary retention (n = 3; 16%), tachycardia (n = 7; 36%) and repeated vomiting (n = 1; 5%). Three patients received SDAC. All patients with pathological ECG findings also showed other clinical symptoms. No severe or fatal cases were reported.
Conclusion: The toxicity profile of escitalopram seems to be favorable in acute overdose, as no severe or fatal cases were registered. Overdoses resulted predominantly in mild symptoms, especially affecting the central nervous and gastrointestinal systems. Mild to moderate QTc prolongation, but no episodes of torsade de pointes were observed. In our series, clinically asymptomatic patients with reported ECG findings did not show QTc prolongation.

249. Different courses of quetiapine poisoning in two patients with gastric decontamination

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Objective: Quetiapine is widely used as an antipsychotic drug and intoxications with this substance are relatively common. In addition, pharmacobezoars after ingestion of large doses of extended-release (XR) quetiapine have been reported [1]. Therefore it is important to know the formulation in order to adapt poison centre recommendations regarding treatment and duration of monitoring of the poisoned patient. We report two

poisoning cases with high doses of XR quetiapine showing very different courses subject to the completeness of gastric decontamination.

Case reports: Case 1. A 48-year-old female ingested 18.2 g of XR quetiapine in a suicide attempt. Activated charcoal (AC) was given (pre-hospital) to the still alert patient. In hospital, gastroscopy was performed and a massive "lump" observed, but only about one tenth of it could be removed within 2.5 hours. Consequently, AC was administered repeatedly. Within 24 hours of ingestion, however, the patient became comatose and required mechanical ventilation. She remained in intensive care for a total of 4 days. Case 2. A 31-year-old female ingested 14 g of XR quetiapine plus 3 g of immediate release quetiapine in a suicide attempt. She was slightly somnolent upon admittance to hospital, and gastroscopy was performed immediately. A large conglomerate was found in the stomach, which could be removed almost completely (estimated 95%) within 3 hours. The patient was transferred to intensive care unit (ICU), where she became awake within another 4 hours and wanted to leave the hospital.

Conclusion: In both cases the same procedures were performed, although gastroscopic removal was incomplete in case 1. We observed a significant difference in severity and duration of symptoms. Despite repeated application of AC, patient 1 became comatose and had to be monitored in ICU for 4 days. In contrast, patient 2 had a much faster recovery. Although it is not known how often AC was given, it seems to have been of little benefit for the clinical course in patient 1. These cases show that an almost complete removal of the agglomerate from the stomach is associated with a significantly faster recovery, regardless of the administration of AC. It therefore seems reasonable to take this into consideration and to recommend removing the whole conglomerate in large overdoses of XR quetiapine.

Reference

[1] Rauber-Lüthy C, Hofer KE, Bodmer M et al. Gastric pharmacobezoars in quetiapine extended-release overdose: a case series. Clin Toxicol (Phila). 2013;51:937–940.

250. The association between phenytoin (diphenylhydantoin) and permanent cerebellar damage

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Objective: To review reports of cerebellar damage judged radiologically and by clinical signs following exposure to phenytoin.

Methods: A systematic review of Medline and EMBASE using search terms (phenytoin or diphenylhydantoin or Dilantin® or DPH).mp. AND (cerebellum or cerebellar).mp. limited to human and adverse effects.

Results: Of 765 references, 67 appeared relevant from the title or abstract; 51 publications reported case(s), and referred to a further 18 reports. Altogether 89 cases were identified (Table 1). On radiology, 10 patients showed no cerebellar abnormalities; 48 had evidence of cerebellar atrophy, often only at follow-up; and 1 scan showed a cerebellar infarct. Clinical signs of cerebellar dysfunction resolved in 10 patients who had radiological studies: radiology showed no abnormality in 3, but signs of cerebellar atrophy in 6 and cerebellar infarction in 1. Of 8 patients who had no cerebellar abnormality on radiology, four had residual signs (2 died during the acute episode). This is consistent with radiological studies of patients on long-term phenytoin treatment, in which there is no concordance between cerebellar atrophy on scans and clinical cerebellar signs [1]. In all 10 reported cases, neuro-histopathology demonstrated loss of cerebellar Purkinje cells.

Table 1. Data extracted from 89 case reports of cerebellar dysfunction associated with phenytoin exposure.

Parameter	Number of reports	Number of cases with data
All cases with some data	–	89
Patient data		
Number of females	46	–
Median age (range) years	27 (2.7–78)	82
Acute or subacute exposure with or without chronic exposure	13	86
Chronic (> 8 week) exposure	73	86
Clinical signs		
Ataxia at presentation	75	80
Dysarthria at presentation	48	80
Nystagmus at presentation	55	80
Ataxia, dysarthria, and nystagmus	38	80
Phenytoin concentration		
Median peak phenytoin concentration (range) mg/L	50 (8–128)	49
Outcome		
No residual cerebellar signs	13	63
Some improvement in signs	31	63
No improvement in signs	14	63
Progression of signs	5	63

Conclusion: Most of the cases of cerebellar signs that persist after exposure to phenytoin have been reported in patients exposed to high doses or high concentrations, often for more than two months. Ataxia is the commonest sign recorded at presentation, with or without dysarthria and nystagmus. Most patients improve after phenytoin treatment is withdrawn; 20% resolve completely. Signs can progress, especially if patients are still exposed to phenytoin. Radiological evidence of cerebellar damage correlates poorly with the presence of physical signs.

Reference

[1] Del Negro A, Danatas CD, Zanardi V, et al. [Dose-dependent relationship of chronic use of phenytoin and cerebellar atrophy in patients with epilepsy]. Arquiv Neuro-Psiquiatria. 2000;58 276–281. Portuguese.

251. Cardiac tamponade in acute-on-chronic clozapine intoxication: the key role of bedside echocardiography

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Objective: Point-of-care echocardiography has the unique ability to screen for unexpected structural findings in critically ill patients. Clozapine is a very effective atypical antipsychotic used most frequently in the management of treatment-resistant

schizophrenia but it may be associated with a number of risks, such as agranulocytosis, seizures, polyserositis and cardiovascular adverse effects including QTc prolongation and, more rarely, myocarditis and pericarditis. In the setting of acute overdose the majority of patients suffer only from changes of mental status and alteration of consciousness, often combined with mild anticholinergic syndrome with sinus tachycardia and slight hypotension. We report a case of life-threatening pericarditis caused by intentional clozapine overdose and treated with supportive care and pericardiocentesis guided by performing bedside echocardiography.

Case report: A 38-year-old woman with a history of schizophrenia presented at our department with a comatose mental status. According to her parents approximately 2-4 hours earlier she had intoxicated herself with her maintenance oral medication clozapine. On admission her Glasgow Coma Score was 5, her blood pressure (BP) 103/67 mmHg and her heart rate 116 bpm. She was intubated, mechanically ventilated and was put on supportive care. Her electrocardiogram (ECG) was normal except for a mildly lengthened QTc of 460 ms. Several hours later she developed a marked sinus tachycardia (160-170 bpm) and hemodynamic compromise with a BP of 70/50 mmHg, signs of peripheral hypoperfusion and her ECG confirmed low voltage. A bedside echocardiography revealed a large pericardial effusion with undoubted evidence of cardiac tamponade. After temporizing measures of volume resuscitation and vasopressor therapy, a life-saving pericardiocentesis was carried out guided by echocardiography. After the removal of the pericardial fluid the patient's state improved dramatically and she fully recovered along with the cessation of clozapine therapy and without NSAID or colchicine therapy. Further laboratory evaluation failed to reveal an unequivocal infectious or non-infectious cause of pericarditis in the background. Serum clozapine and N-desmethylclozapine concentrations were not determined. According to the Naranjo probability scale and the Drug Interaction Probability Scale there was a probable relationship, score 6 and 5, respectively, between the development of pericarditis and clozapine overdose in this patient.

Conclusion: Acute clozapine overdose can cause life-threatening serositis and cardiac tamponade. In this setting point-of-care echocardiography is the method of choice to visualize and judge it and to guide life-saving pericardiocentesis.

252. Acute kidney failure due to acetaminophen overdose: a case report

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Objective: To raise awareness for the rare, but clinically important nephrotoxicity associated with acetaminophen overdose. Only few cases of acute kidney failure after acetaminophen intoxication are reported and none of them had an increase of creatinine of more than 10 mg/dL.

Case report: A 23-year-old man presented to the emergency department with epigastric complaints 24 hours after ingestion of 10 g of immediate release acetaminophen over a 6 hour period. Further clinical examination was unremarkable. Initial lab work-up showed elevated liver function tests (AST 496 U/L, ALT 736 U/L, LDH 557 U/L and γGT 152 U/L). Renal function was normal with creatinine concentration 0.66 mg/dL and estimated glomerular filtration rate (eGFR) (CKD-EPI) > 60 mL/min/1.73 m^2. Coagulation tests were also disturbed (INR 1.44). Initial toxicology 23 hours after intoxication showed a serum acetaminophen level of 28.6 mg/L. Based on the Rumack-Matthew nomogram, a predictor of acetaminophen-induced hepatotoxicity, he was started on intravenous N-acetylcysteine therapy. Further toxicological work-up showed, beside the presence of acetaminophen, a negative urine analysis. He was transferred to the intensive care unit (ICU) for further investigation. Two days after admission at the ICU, kidney function decreased rapidly with a peak creatinine concentration of 13.9 mg/dL and eGFR 4.4 mL/min/1.73 m^2 nine days after intoxication and hemodialysis was started. No improvement of kidney function was observed ten days after intoxication and renal biopsy was performed which showed acute tubular necrosis with oedema due to acetaminophen toxicity. One week after release from the hospital, kidney function improved with a serum creatinine of 1.62 mg/dL and eGFR (CKD-EPI) 58.9 mL/min/1.73m^2.

Conclusion: Acetaminophen-associated liver damage is more recognized than kidney toxicity, but renal insufficiency occurs in <2% of patients with acetaminophen overdose [1]. The mechanism of acetaminophen toxicity is well described in the liver, but is less clearly understood in the kidney [2]. Possible mechanisms include the cytochrome P-450 pathway, the prostaglandin synthase end deacetylase enzymes [3]. In conclusion, we want to emphasize the importance of considering nephrotoxicity as a rare, but clinically important, complication of acetaminophen intoxication.

References

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[3] Bessems JG, Vermeulen NP. Paracetamol (acetaminophen-) induced toxicity: molecular and biochemical mechanisms, analogues, and protective approaches. Rev Toxicol. 2001;31:55–138.

253. Venlafaxine-associated hypoglycemia: frequency and correlation with symptom severity

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Objective: Venlafaxine, an antidepressant of the noradrenaline and serotonin reuptake inhibitor class, has been reported to cause hypoglycemia in overdose in four published cases [1]. In contrast, available data from animal and clinical investigations suggests venlafaxine does not affect glucose homeostasis at therapeutic doses [2]. To this date, studies further characterising hypoglycemia in venlafaxine overdose are lacking. We aimed to investigate the frequency at which this phenomenon occurs and whether it was correlated with symptom severity.

Methods: We retrospectively analysed clinical records including blood glucose measurements (BG) in all patients with an analytically confirmed venlafaxine overdose treated at our institution between January 2008 and August 2019. Multi-drug exposures were included. Symptom severity was assessed using the Poisoning Severity Score (PSS). Statistical comparisons were made using an unpaired t-test and Spearman's rank correlation coefficient.

Results: Overall, 85 cases of analytically confirmed venlafaxine poisonings were identified, of these, 16 were single substance ingestions. Hypoglycemia occurred in 31.8% (27/85) of all venlafaxine poisonings and in 31.3% (5/16) of single substance ingestions. Twenty patients (23.5%) exhibited mild hypoglycemia (BG 50-70 mg/dL), 7 (8.2%) had moderate hypoglycemia (BG 30-50 mg/dL) and no patient was severely hypoglycemic (BG ≤30 mg/dL). The mean minimum BG was significantly lower in severely poisoned patients (PSS 3, 16 patients, BG 62 mg/dL) than in mildly to moderately poisoned patients (PSS 0 to 2, 69 patients, BG 86 mg/dL) ($p < 0.0001$). The minimum BG exhibited a significant moderate negative correlation with symptom severity ($r = -0.448$, $p < 0.0001$), the occurrence of seizures ($r = -0.341$, $p = 0.001$), the reported dose ingested where available ($r = -0.482$, $p = 0.0001$) and the peak venlafaxine concentration in the serum where available ($r = -0.469$, $p = 0.008$).
Conclusion: A mild to moderate hypoglycemia can be observed in up to a third of venlafaxine overdoses. The similar rates of hypoglycemia between single and multiple substance ingestions indicate that the phenomenon might be directly attributable to venlafaxine. Lower blood glucose concentrations appear to correlate with more severe presentations.

References

[1] Brvar M, Koželj G, Mašič LP. Hypoglycemia in venlafaxine overdose: a hypothesis of increased glucose uptake. Eur J Clin Pharmacol. 2015;71:261–262.
[2] McIntyre RS, Soczynska JK, Konarski JZ, et al. The effect of antidepressants on glucose homeostasis and insulin sensitivity: synthesis and mechanisms. Expert Opin Drug Saf. 2006;5:157–168.

254. Hydroxyzine poisoning in the intensive care unit: predictive factors of cardiovascular complications and toxicokinetics

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Objective: Despite its wide use as an antihistaminic and anxiolytic drug, only rare hydroxyzine poisonings have been reported and almost all reported cases led to fatality. Therefore, we designed this study to describe the clinical features resulting from hydroxyzine overdose; to evaluate the prognosticators on admission; and to describe the toxicokinetics of hydroxyzine in overdose.
Methods: We conducted a retrospective single-centre observational study including all hydroxyzine poisoning cases (defined as poisoned patients with serum hydroxyzine concentration >1 mg/L on admission) admitted to our intensive care unit (ICU) in 2012-2019. The predictive parameters were studied using univariate comparisons (performed with Mann-Whitney and chi-squared tests, as required) and toxicokinetics using a non-compartmental approach. Correlations were tested using Bartlett's sphericity tests and the Spearman coefficients were determined.
Results: Fifty-nine hydroxyzine-poisoned patients (31 females/28 males; age 41 years [30-50]; median [25th-75th percentiles]]) were included. Hydroxyzine was included in the patient's long-term treatment in almost half of the cases. Poisoning resulted from multidrug ingestion (75%). The presumed ingested dose of hydroxyzine was 750 mg [250-1,437] and the serum concentration on admission was 0.43 mg/L [0.30-1.06] with limited correlation between these two parameters ($R^2 = 0.368$; $p = 0.001$). The most frequently observed complications included aspiration pneumonia (39%), cardiovascular failure (29%), rhabdomyolysis (10%), renal failure (2%), liver injury (5%) and fatality (1 patient, 2%). Based on univariate analyses, the predictive factors on ICU admission of the risk of cardiovascular failure were the depth of consciousness impairment ($p = 0.0007$), the onset of hypotension ($p = 0.007$) and the severity of lactate increase ($p = 0.03$). There was a non-significant trend for an association between the ingested dose and the risk of cardiovascular failure ($p = 0.07$), while serum hydroxyzine concentration was not predictive. Hydroxyzine elimination half-life was 17.6 hours [16.9-38.0], its volume of distribution 2233 L [1596; 4306] and its apparent clearance 49.6 L/h [30.1; 184.9].
Conclusion: Hydroxyzine poisoning may be life-threatening requiring ICU admission. The presumed ingested dose but not the serum concentration on admission tends to be associated with the risk of cardiovascular failure onset. The elimination half-life does not significantly differ from the values measured at pharmacological doses (approximately 14 hours, range 7-20 hours).

255. Lamotrigine poisoning in the ICU: a case series with evaluation of the toxicokinetics and the predictive value of the plasma concentration on admission

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Objective: Lamotrigine is increasingly used as treatment for epilepsy and bipolar disease. Lamotrigine overdoses (generally known as relatively mild in the literature) are increasingly admitted to the intensive care unit (ICU). Our aim was to report a series of severe lamotrigine poisoning cases admitted to the ICU; to investigate the predictive value of plasma lamotrigine concentration on admission; and to determine its pharmacokinetic parameters.
Methods: We conducted a retrospective single-centre observational study including all lamotrigine-poisoned patients (as defined by the measurement of at least one plasma concentration >15 mg/L, measured using liquid chromatography coupled to mass spectrometry) admitted to the ICU in 2011-2019. Comparisons between the patient groups were performed using Mann-Whitney tests and correlations using Bartlett's sphericity tests with the calculation of the Spearman coefficients.
Results: Fifteen lamotrigine-poisoned patients (7 females/8 males, aged 43 years [32-49] (median [25th-75th percentiles]) were included. Poisonings were multidrug ingestions involving four [3-5] toxicants. On admission, the Glasgow Coma Score was 7 [3-15], justifying tracheal intubation in 67% of the cases. The complications included aspiration pneumonia (53%), vomiting (47%), cardiovascular failure (40%), rhabdomyolysis (27%), seizures (13%), membrane stabilizing effects on the electrocardiogram (ECG) (13%) and fatality (7%). The presumed ingested dose and the plasma concentration of lamotrigine on admission were 3.6 g

[1.0-5.7] and 25.8 mg/L [17.3-35.0], respectively and did not significantly correlate. No significant relationships existed between the ingested dose or plasma concentration of lamotrigine on admission and the different parameters of clinical severity including the Glasgow Coma Score, the onset of seizure, the requirement of mechanical ventilation and the need for catecholamine administration. Based on a non-compartmental approach, we determined the toxicokinetic parameters of lamotrigine including its elimination half-life of 33.1 hours [26.5-47.2], its distribution volume of 241 L [137-371] and its apparent clearance of 6.3 L/h [2.8-9.7].
Conclusion: Lamotrigine poisonings may be responsible for life-threatening features requiring ICU admission. The plasma concentration on ICU admission is not helpful to predict the risk of complications. The half-life of elimination in overdose is in the range of the values reported at pharmacological doses (14-110 hours).

256. Risperidone poisoning in the intensive care unit: evaluation of the poisoning severity on admission

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Objective: Risperidone, a second generation antipsychotic drug, is increasingly prescribed to treat schizophrenia and bipolar disease. Severe risperidone poisonings have been rarely reported. Our objective was to describe the poisoning-related clinical features; to investigate the prognostic value of the presumed ingested dose and the plasma concentration of risperidone on admission; and to determine the pharmacokinetic parameters in overdose.
Methods: We conducted a retrospective single-center observational study including all risperidone-poisoned patients (defined using serum concentration >0.09 mg/L on admission using liquid chromatography coupled to mass spectrometry) admitted to the intensive care unit (ICU) in 2009-2019. We performed univariate analyses (Mann-Whitney and chi-squared tests, as requested) for subgroup comparisons, Bartlett's sphericity tests with determination of Spearman coefficients to investigate the correlations between the quantitative parameters and a non-compartmental analysis to determine the pharmacokinetic parameters.
Results: Nineteen risperidone-poisoned patients (10 males/9 females; aged 40 years [31-53] (median [25th-75th percentiles]) were included. Risperidone ingestion was mainly in relation to multidrug ingestion in suicide attempts (96%). The presumed ingested dose was 107 mg [46-120] and the serum concentration on admission 0.235 mg/L [0.160-0.500]. The Glasgow Coma Score on admission was 7 [3-14]. The main clinical features associated with coma were pupil abnormalities (44% miosis/11% mydriasis), QT prolongation on the ECG (21%), pyramidal syndrome (19%), vomiting (11%), myoclonus/dyskinesia (5%) and typical anticholinergic syndrome (5%). Management included mechanical ventilation (58%), catecholamine infusion (23%) and activated charcoal administration (16%). The main observed complications included aspiration pneumonia (63%), cardiovascular failure (23%), rhabdomyolysis (21%), acute respiratory distress syndrome (21%), acute liver injury (11%) and renal failure (5%). No death occurred. No significant correlation was observed between the presumed ingested dose and the serum concentration on admission versus the different parameters of severity (Glasgow Coma Score, QT duration, mechanical ventilation requirement and catecholamine infusion). Risperidone half-life of elimination was included in the range of pharmacological doses (3-17 hours).
Conclusion: Rispiridone poisoning may result in life-threatening presentations, requiring ICU admission. Risperidone concentration on admission does not predict the onset of complications.

257. Nicardipine poisoning in the intensive care unit: management, outcome and toxicokinetics

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Objective: Acute nicardipine poisonings have been rarely reported. Nicardipine, a dihydropyridine derivate with potent vasodilatation effects, is able to induce cardiovascular failure in overdose. Our objectives were to describe the clinical features of nicardipine poisoning; to report patient management and outcome; and to investigate nicardipine toxicokinetics and its predictive value on admission.
Methods: We conducted a single-center observational study including all nicardipine-poisoned patients admitted to the intensive care unit (ICU) in 2013-2019. We performed univariate analyses (Mann-Whitney and chi-squared tests, as requested) for subgroup comparisons, Bartlett's sphericity tests with determination of Spearman coefficients to investigate the correlations between the quantitative parameters and a non-compartmental analysis to determine the pharmacokinetic parameters.
Results: Eighteen patients (8 females/10 males, aged 60 years [40-74] (median [25th-75th percentiles])) were included. On admission, the patients presented tachycardia (40%) and hypotension (50%). The presumed ingested dose and serum concentration of nicardipine on admission were 1,000 mg [700-2,700] and 308 ng/mL [209-563], respectively. Supportive treatments included fluids (100%), mechanical ventilation (44%), norepinephrine (50%), dobutamine (28%), epinephrine (17%), isoprenaline (11%), glypressin (11%) and methylene blue (11%). The administered antidotes included calcium salts (78%), euglycemic insulin (39%) and glucagon (6%). extracorporeal membrane oxygenation (ECMO) and albumin dialysis (molecular adsorbent recirculating system, MARS®) were performed in 17% of the cases. Complications included cardiovascular failure (50%), aspiration pneumonia (33%), atrioventricular block (17%), hospital-acquired infections (6%) and death (11%). The ingested dose but not the concentration of nicardipine on admission were correlated to poisoning severity represented by the elevation in blood lactate ($p = 0.005$), serum ionized calcium ($p = 0.05$), blood glucose ($p = 0.01$) and brain natriuretic peptide (BNP, $p = 0.006$). The elimination half-life of nicardipine was significantly prolonged (10.5 hours [9.7-14.5]) in comparison to the pharmacological conditions (2-4 hours).
Conclusion: Despite expected limited direct cardiac toxicity, nicardipine may be responsible for severe and even fatal complications in overdose. Its elimination half-life is dose-dependent, however, in contrast to the ingested dose, the serum nicardipine concentration does not predict the poisoning severity.

258. Poisonings involving angiotensin-converting enzyme inhibitors in the intensive care unit: a case series

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Objective: The angiotensin-converting enzyme (ACE) inhibitors are increasingly prescribed to treat hypertension, and are thus responsible for increasing poisoning cases, however, the clinical data regarding the toxicity of ACE inhibitors remain limited. Our objectives were to describe the clinical features attributed to ACE inhibitor poisoning and report the patient management and outcome.
Methods: We conducted a single-center observational study including all ACE inhibitor-poisoned patients admitted to the intensive care unit (ICU) in 2013-2019. We performed univariate analyses (Mann-Whitney and chi-squared tests, as requested) for subgroup comparisons. The toxicokinetics was modelled in two cases based on a non-compartmental model.
Results: Thirty-three patients (14 females/19 males; age 56 years [48-73] (median [25th-75th percentiles])) were included. The poisoning was related to a voluntary multidrug ingestion (97%, with one additional cardiotoxicant drug) in 81% of the cases. Ramipril (48%, 63 mg [25-300]) and perindopril (33%, ingested dose, 180 mg [125-300]) were the two most frequently involved ACE inhibitors. Clinical features included hypotension (88%), shock (72%), consciousness impairment (24%, Glasgow Coma Score on admission, 14 [12-15]), hyperkalemia (9%) and renal failure (6%). The patients received fluids (85%) vasopressors (72%), mechanical ventilation (54%), charcoal (30%) and extracorporeal membrane oxygenation (ECMO) (12%). Two fatalities occurred in relation to cardiac arrest. There were no significant differences regarding the clinical presentation, the severity and the outcome when comparing ramipril versus perindopril. The toxicokinetics of perindopril (half-life: 1 hour), ramipril (5 hours) and their respective metabolites, perindoprilate (23 hours) and ramiprilate (25 hours) was studied in two cases, demonstrating marked prolongation in drug elimination in the presence of renal failure (case of perindopril poisoning).
Conclusion: ACE inhibitor overdose frequently involves one additional cardiotoxicant and may result in severe and even fatal outcome. Clinical features mainly include vasoplegic shock. Our findings do not support the existence of differences between the different ACE inhibitor compounds. Drug elimination is prolonged in patients with renal failure.

259. Salicylate poisoning admitted to the intensive care unit: features and toxicokinetics

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Objective: Adult salicylate poisoning is now relatively rare in France. Toxicity is mainly related to the alterations in the acid/base balance and to renal function impairment following the ingestion of doses >10 g. Our objective was to report a case series of moderate to severe salicylate poisonings admitted to the intensive care unit (ICU) and investigate salicylate toxicokinetics and its relationships to clinical features.
Methods: We conducted a retrospective single-centre observational study including all salicylate-poisoned patients with documented plasma concentrations admitted to the ICU in 2007-2019. Correlations between the different quantitative parameters were tested using Bartlett's sphericity tests and the Spearman coefficients were determined. Salicylate toxicokinetics was studied using a non-compartmental approach.
Results: Thirty-seven patients (22 females/15 males, aged 33 years [23-55] (median [25th-75th percentiles])) were included. The patients presented a past history of depression (60%) and suicide attempt (41%). The co-ingested toxicants included psychotropic drugs (40%), ethanol/recreational drugs (15%), analgesics (14%) and/or cardiotoxicants (12%). The presumed ingested dose was 20.0 g [7.7-30.0]. The salicylate concentration on admission was 418 mg/L [187; 506]. The clinical features included dehydration (65%), hypoacusis (30%), vomiting (27%), abdominal pain (19%), nausea (11%) and seizures (3%). The majority of the patients exhibited respiratory alkalosis [arterial pH 7.48 [7.42-7.52] and $PaCO_2$ 36 mmHg [29-41], with significant but weak correlation with salicylate concentrations ($R^2 = 0.32$, $p = 0.006$)] but no significant increase in the anion gap (11.8 mmol/L [9.1; 15.7]). These findings supported the relatively short delay between the ingestion and patient admission (7 h [4-11]), in this series. One patient developed marked metabolic acidosis. Patients were treated with alkalinization (70%), activated charcoal (36%), mechanical ventilation (11%), gastric lavage (3%) and/or catecholamine infusion (3%). No patient died in the ICU. Using a non-compartmental approach, salicylate elimination half-life was 6.7 h [5.8-11.7], its volume of distribution 25.9 L [19.1-20,.2] and its clearance 1.6 L/h [1.0-3.2].
Conclusion: Salicylate intoxication may be life-threatening, however managed without delay (mainly using alkalinization), the metabolic complications are limited. In these conditions, the toxicokinetics of elimination are dose-dependent.

260. Antidepressant drug poisonings and the risk of thromboembolic complications: a case series from an intensive care unit

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Objective: Antidepressant drugs have been increasingly prescribed during the last ten years, resulting in increasing self-poisonings with these drugs. Interestingly, a possible enhanced risk of venous thromboembolic complications (VTEC) has been reported in patients treated with antidepressant drugs; however, no study has investigated such a risk in overdose patients who have ingested large amounts of these drugs. Our objective was to describe the circumstances and consequences of VTEC onset in the patients severely poisoned with antidepressant drugs.
Methods: We conducted a retrospective single-centre cohort study including all antidepressant drug-poisoned patients who were admitted to the intensive care unit (ICU) and developed VTEC (thrombophlebitis and pulmonary edema or both) during their stay in 2012-2019.
Results: Fourteen antidepressant drug-poisoned patients [11 females/3 males; age 50 years (43-57) (median (25th-75th

percentiles); past history of depression, 92%] developed VTEC during their ICU stay (thrombophlebitis 29%, pulmonary embolism 29% and both 42%). The prevalence was estimated at approximately 5.3% (among the 262 ICU poisoned patients who presumably ingested toxic doses of antidepressant drugs). The antidepressant drugs involved were tricyclic antidepressants (64%), norepinephrine and serotonin reuptake inhibitors (21%) or selective serotonin reuptake inhibitors (7%). The patients were found comatose lying in supine position (71%) with Glasgow Coma Score of 3 (3-12). On admission, the routine hemostasis tests including activated partial thromboplastin time, prothrombin time index and platelet count were in the normal range. All these patients received an initial preventive dose of enoxaparin. VTEC was diagnosed with a 7-day delay after the drug ingestion and initial treatment with non-fractionated heparin. ICU stay was prolonged to 12 days (6-20). No patient died. Confounding factors could not be definitively eliminated (e.g. past history of VTEC 14%; cancer 7%).
Conclusion: Our findings suggest a possible association between antidepressant poisonings (mainly with tricyclic antidepressants) and VTEC onset. However, due to the absence of control group, the retrospective design of our study and the major variability of VTEC prevalence in published studies depending on the case-mix, the diagnostic methods used and the use of prophylactic drugs [1], further studies are required for a definitive conclusion.

Reference

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261. Massive polypharmacy overdose resulting in diltiazem pharmacobezoar formation

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Objective: To describe a case of diltiazem pharmacobezoar formation after a massive polypharmacy ingestion.
Case report: A 74-year-old female with a history of depression, bipolar, prior suicide attempt, hypertension, hyperlipidemia, and gastroesophageal reflux disease presented to the emergency department approximately 1 hour after an intentional ingestion of all her medications. Her medication list included diltiazem extended release, fluoxetine, ibuprofen, pravastatin, ranitidine, omeprazole, lisinopril and aspirin. At the time of presentation to the hospital patient was awake, alert and oriented, but slightly somnolent. Early in her hospital course she had several episodes of large volume emesis containing exclusively pills and pill fragments. Examination of the vomitus revealed two large pharmacobezoars. The content of the bezoars appeared to be undigested diltiazem capsules coalesced with partially digested ranitidine tablets. It did not appear that any of the other xenobiotics ingested had been involved in the bezoar formation. Her vital signs at presentation were heart rate 72 beats/minute and blood pressure 121/72 mmHg. Her initial electrocardiogram showed a first degree atrioventricular block with a PR interval of 264 ms. Approximately 80 minutes after the initial electrocardiogram, a second electrocardiogram showed normal sinus rhythm with a Mobitz type I second degree atrioventricular block. At this point, it was decided to prophylactically perform tracheal intubation and a gastric lavage followed by whole bowel irrigation with polyethylene glycol through an orogastric tube. In addition 3 g of calcium gluconate and isotonic fluids were also given intravenously. She was admitted to the intensive care unit where her vital signs started to decompensate. Additional interventions included atropine, calcium chloride, glucagon, high dose insulin euglycemic therapy, transcutaneous pacing, vasopressor support with vasopressin, epinephrine, and norepinephrine. The patient continued to deteriorate resulting in an episode of pulseless electrical activity less than 12 hours after the estimated time of ingestion. At this point, she received high quality cardiopulmonary resuscitation and intravenous lipid emulsion therapy but despite resuscitative efforts she did not survive.
Conclusion: The poor prognosis associated with extended release calcium channel blocker overdoses is well recognised. This case report highlights the unique situation of pharmacobezoar formation that can be associated with diltiazem overdoses which can prolong the absorptive phase of the medication. Providers should be aware of the need to treat patients earlier and more aggressively should pharmacobezoars be found in their vomitus.

262. Lurasidone mono-ingestion overdoses: a case series with minimal toxicity

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Objective: Lurasidone is a second-generation antipsychotic agent used to treat schizophrenia. In therapeutic doses it has few reported side-effects, less weight gain than other similar agents and little effect on the electrocardiogram (ECG). Currently, data are lacking regarding toxicity after lurasidone mono-ingestion overdoses. We describe clinical and electrocardiographic features in a series of lurasidone mono-ingestion overdoses.
Methods: Retrospective case series of self-reported lurasidone overdoses treated by the Monash Health toxicology unit between 2016 and 2019. Polydrug ingestions including lurasidone with other drugs that affect cardiac conduction or conscious state were excluded. Data collected included age, gender, dose of lurasidone ingested (in mg and defined daily doses [DDD]), vital signs and conscious state, time to lowest Glasgow Coma Score (GCS), duration of sedation, complications (e.g. hypotension, seizures) and electrocardiographic abnormalities (rhythm, QRS, QT-heart rate pairs, QTc-Fredericia) on serial ECGs.
Results: Six patients with mono-ingestion overdose of lurasidone were identified. Sixty-six percent ($n = 4$) were female, median age: 31 years (range: 16-44 years), median reported ingested dose 820 mg (range: 300-2000 mg), 5 DDDs (range: 1.5-11). Median lowest GCS 14 occurred at 2.6 hours (GCS range 12 to 15; time range 2–9.5 hours) post-ingestion. Hypotension was observed in two patients (median systolic blood pressure (SBP) 95 mmHg, responsive to fluid). Transient tachycardia was observed in one patient (median 103 bpm, range: 85-112). Median heart rate for all patients was 75 bpm (range: 50-112). No patients displayed anticholinergic signs. There were no reports of mydriasis, urinary retention or delirium. A total of 13 ECGs were recorded from 1.1 to 15 hours post-ingestion. Median number of ECGs per patient was two. Median QTc-Fredericia was 425 ms (range: 360-475 ms). When measured QT-heart rate pairs were plotted on the QT-nomogram, none crossed the nomogram line. Pre-overdose ECGs were available for three patients. QT-intervals were similar to post-overdose ECGs. There was no evidence of any other conduction or rhythm disturbances.

All patients were admitted to the toxicology observation unit. Median hospital length of stay was 14.4 hours (range: 7.4-22 hours). There were no complications or deaths in this cohort.
Conclusion: In this small cohort, isolated lurasidone overdose resulted in mild sedation and minimal ECG interval effects. We did not observe any anticholinergic toxicity seen commonly after overdose with other newer antipsychotics, such as quetiapine and olanzapine. Larger case series are required to further ascertain incidence of features of toxicity.

263. Combined beta-blocker and beta-agonist drugs overdose: an unusual balance

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Objective: Multidrug overdose can pose a life-threatening risk, especially with cardiovascular medications. In overdose, the expected typical syndromes may be less clear because of the opposite action of other drugs taken concomitantly, and the final clinical presentation can be atypical and unexpected. We report an unusual case of mixed overdose due to propranolol and an inhalatory combined beta-agonist/corticosteroid drug.
Case report: A 21-year-old female, 45 kg, was admitted to the emergency department three hours after the ingestion of her mother's propranolol (30 × 40 mg tablets) and inhalation of 50 puffs of her own beclomethasone/formoterol (100 µg/6 µg) in a suicidal attempt. She denied consumption of other medications, alcohol or drugs of abuse. She had a history of asthma but no pre-existing psychiatric illness. Upon arrival, she was fully conscious, oriented and co-operative; her vital signs were normal. Her physical examination and laboratory investigations were unremarkable. No evidence of alcohol, barbiturates, benzodiazepines, or tricyclic antidepressants was found in the serum. The baseline 12-lead electrocardiogram was normal. During initial clinical examination, the patient experienced transient visual hallucinations involving a tiger, a dog, and a child; she reported they were walking in the emergency room. She was always critical regarding her visual hallucinations. Gastrointestinal decontamination was undertaken and cardiovascular monitoring started. During the 24 hour-observation period, the patient remained awake, and free of cardiovascular effects despite serum propranolol concentrations of 781 ng/mL (therapeutic range 20-300 ng/mL) in the blood sample taken at admission. No electrocardiogram modifications, decreased blood pressure, nor heart rate changes were recorded. No episodes of bronchospasms occurred. No further hallucination episodes were reported. She was discharged asymptomatic the day after admission.
Conclusion: Beta-blocker poisoning is characterized by severe bradycardia and hypotension, while in beta-2 agonist overdose tachycardia and tremors are commonly observed. In our case there was a lack of cardiovascular effects despite the significant amounts of medications taken, and this was probably due to the unusual association of substances with opposite and antagonistic actions. By contrast, the patient developed visual hallucinations that can be related to propranolol central nervous system effects. Propranolol is a lipophilic compound that rapidly crosses the blood-brain barrier and reaches concentrations in the brain up to ten times the plasma concentrations. Based on these findings, we assumed that the hallucinations were associated with elevated concentrations of propranolol in the brain.

264. Characteristics of use and outcome of naloxone administration to non-intensive care and non-surgical hospitalized adult patients: a pilot study

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Objective: To evaluate the characteristics of use and outcome of hospitalization-related naloxone administrations in adult patients.
Methods: A single medical center retrospective review of electronic medical records of naloxone administrations during hospitalizations, between January 1 to December 31, 2018. Exclusion criteria were age under 18 years, naloxone administration within the first 24 hours of hospitalization and administrations in the emergency department, operating theater, recovery room, or intensive care units. Eligible records were manually screened. Data collected included demographic and clinical variables. Descriptive statistical analysis was performed.
Results: Of about 10,000 hospitalizations, 9 patient records (0.09%) were retrieved and included after screening; 5 male and 4 female. Average age was 73 years (range 29-91). Three patients (33%) had chronic pain, 2 had severe respiratory disease, 2 had major cardiac illness and 2 had significant neurologic impairment. The indication for naloxone administration was reduced consciousness in all cases. In one case the patient also had respiratory deterioration and in another case hemodynamic instability was recorded. Miosis was recorded in one case. In all cases the medical team suspected opioid exposure. In 6 cases (66%) there was a record of a relevant medication given before the worsening of the patient; 2 were treated with IV tramadol, 2 with oral oxycodone and 2 with buprenorphine transdermal patch. In 3 cases, a clear overdose was given: oxycodone duplication error and wrong tramadol and buprenorphine doses. Naloxone was given in IV boluses. In 7 cases only a single dose was administered; in the other 2 cases there were 2 and 3 naloxone administrations. The dose was 0.4 mg in 8 cases and 0.2 mg in one case. Significant clinical improvement was recorded in only 3 cases and partial improvement in 2 cases. Hospital mortality was recorded in 4 (44.4%) cases.
Conclusion: Naloxone administration during hospitalization, not related to emergency departments, operating theaters, recovery rooms, or intensive care units is rare. In these few cases, naloxone administration is mainly secondary to reduction of consciousness with suspected opioid medication exposure with limited clinical assessment before treatment and partial improvement. Dosing is conservative and confined to one 0.4 mg ampule. As availability of potent narcotics and opioids is expanding and hospitalized patients are older with more comorbidities, better training and preparedness of hospital staff for the proper use of naloxone and adequate patient pre- and post-assessment is essential. Monitoring of naloxone administrations may serve as a trigger tool for medication error identification.

265. Amlodipine overdose presenting with hyponatraemia

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Objective: We report a case of intentional amlodipine overdose who presented with hyponatraemia which was further exacerbated by high dose euglycaemic therapy (HIET).
Case report: An 18-year-old female presented to the emergency department after ingesting 250 mg of amlodipine. On arrival, the vital signs were: blood pressure 90/38 mmHg, heart rate 117 bpm, respiratory rate 18 breaths/minute and oxygen saturation 98% (room air). The blood gas analysis showed: pH 7.460, sodium 131 mmol/L and glucose 5.9 mmol/L. Initial blood tests revealed: sodium 130 mmol/L, potassium 4.1 mmol/L, chloride 99 mmol/L, bicarbonate 22 mmol/L, urea 8.1 mmol/L and creatinine 106 µmol/L. A 2 litre fluid bolus of Ringer's lactate was given. HIET was started ten hours after initial presentation due to worsening hypotension at 3 IU/kg/hour and titrated up to 10 IU/kg/hour to effect with a 50% dextrose infusion running at 40 mL/hour. She was then admitted to high care and HIET continued with mean arterial pressure maintained above 65 mmHg. Serial blood gases revealed a downward trend of sodium values to 118 mmol/L. She was intubated for a decreasing level of consciousness and pulmonary oedema despite fluid restriction. The hyponatraemia was corrected with hypertonic saline: 3 mL/kg over 2 hours and HIET was weaned to 1.5 IU/kg/hour. A work-up was done for hyponatraemia: serum osmolality 277 mmol/kg, urine osmolality 343 mmol/kg and urine sodium 13 mmol/L indicating a hypovolaemic hypotonic hyponatraemia. Serial blood analyses over the next 24 hours showed a rise in sodium to 128 mmol/L. Five days later, HIET and an adrenaline infusion was stopped and the serum sodium had normalised. She was extubated the following day but died due to sepsis in the intensive care unit 12 days later.
Conclusion: This case is unique because the patient had amlodipine-induced hyponatraemia which was further exacerbated by HIET. Hyponatraemia is a rare complication of chronic amlodipine therapy. Amlodipine may induce natriuresis by preventing reabsorption of sodium in the renal tubules [1]. Furthermore, in this case hyponatraemia presented following acute overdose rather than chronic use. Dextrose water is a hypotonic fluid and thus may precipitate hyponatraemia when used as part of HIET. Clinicians should be aware of this potential complication, especially when high doses of HIET are required with increased requirements for dextrose water to combat HIET-induced hypoglycaemia. Hypertonic saline may be considered in severe hyponatraemia.

Reference

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266. Medication errors in nursing homes and other residential institutions with full-time staff attendance: a Danish Poisons Information Centre quality project

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Objective: The Danish Poisons Information Centre (DPIC) receives numerous inquiries concerning medication errors in nursing homes and other residential institutions. The aim of this study was to describe these medication errors and their consequences.
Methods: In the period from 1 March 2018 to 31 March 2019, we prospectively collected data from medication error inquiries from residential institutions with full-time staff attendance. Inquiries from private homes and those concerning non-pharmaceutical exposures and suicide attempts were excluded. For each medication error, the location and type of exposure and DPIC recommendations were registered, and the involved medication was classified according to the anatomical therapeutic classification (ATC).
Results: The DPIC received inquiries fulfilling the study criteria concerning 295 patients (<1% of all DPIC inquiries in the study period). Medication errors had occurred in nursing homes (48%), other residential institutions (51%), or a prison (1%). The medication errors involved the patients' own (51%) or another patients' medicine (49%). Almost half (48%) of medication errors was one-drug exposures, whereas the rest (52%) concerned multidrug exposures. The medication involved in the errors (n = 537), most frequently belonged to ATC-group N (55% of total) - subclassified into antiepileptics (N03, 16%), psycholeptics e.g. antipsychotics and hypnotics (N05, 18%), psychoanaleptics e.g. antidepressants (N06, 10%), analgesics (ATC-group N02, 7%), and antiparkinson drugs (ATC-group NO4, 4%). Medicine used for diseases in the alimentary tract and metabolism (ATC-group A, 14%), the cardiovascular system (ATC-group C, 13%), and for blood and blood forming organs (ATC-group B, 7%) were also frequent. The DPIC recommended hospital admission in 15% and observation at home for 85% of the patients.
Conclusion: Our prospective registration of DPIC inquiries indicate that medication errors in institutions are relatively uncommon but are often complex with multidrug exposures involving other patients' medicines. Most exposures involve medications affecting the central nervous system; and based on risk severity, hospital admission was recommended in almost one sixth of cases. Thus, these results suggest that medication errors in institutions are often serious, and our study points to substantial room for improvement in the handling of medicines in Danish residential institutions.

267. Predictors of intensive care unit admission in pharmaceutical poisoning

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Objective: Acute poisoning is a common cause of emergency department (ED) visits. New data about severity predictor variables could help to be more efficient in reducing morbidity and mortality in poisoned patients [1,2]. The aim of the study was to determine the factors that affect the severity of pharmaceutical-related poisoning in the ED of the Universitari Hospital Son Espases, Palma de Mallorca and the necessity of admission, mainly in the Intensive Care Unit (ICU).
Methods: Patients visiting the emergency department between 2011 and 2018 for drug poisoning were included. A multivariate analysis was performed by a logistic regression to identify the factors that are associated with an increased severity of pharmaceutical poisoning and the need for admission to the ICU.

Results: Of the 2,814 patients with a pharmaceutical-related poisoning between 2011 and 2018, 17.3% patients were admitted to the hospital, 1.3% (n = 37) of which were admitted to ICU. Variables associated with admission were age (OR =1.011; 95% CI: 1.01-1.02), cause of poisoning (suicide, recreational or unintentional) (OR =1.96; 95% CI: 1.51-2.54), the pharmaceutical group, especially insulin (OR =25.8) and biguanides (OR =7.8), which were associated with a higher probability of admission in the ICU. However, we found no relation between calcium antagonists and benzodiazepines poisoning and a higher risk of admission in the ICU. Furthermore, the number of pharmaceuticals involved in poisoning was not associated with a higher admission probability (OR =1.032; 95% CI: 0.93-1.13).
Conclusion: We can consider that insulin and biguanide poisoning are predictors of severity, and they can be related to a further increase in ICU admissions. Benzodiazepines are the most frequent pharmaceuticals involved, but they are not related to an increased severity of poisoning. Poisonings with calcium channel antagonists, despite its known relevance, are not related to increased risk of ICU admission.

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268. Crisis averted? Olanzapine as an antidote for serotonin toxicity: a case report

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Objective: Methylene blue (MB) is sometimes used in the management of toxic vasodilatory shock. However, in simultaneous ingestions of potent serotonergic agents, MB, a MAO-inhibitor, can precipitate life-threatening serotonin toxicity. We describe a case where a severe outcome was possibly averted by the use of olanzapine, an atypical antidepressant with antagonist action at the 5-HT_2 receptor.
Case report: A 70-year-old woman was found obtunded in her home after an overdose of pharmaceuticals. She had access to propiomazine, oxazepam and to her husband's amlodipine, candesartan and citalopram. The poison center was contacted early and gave clinical advice by telephone throughout the course. On admission, the clinical picture was dominated by hemodynamic instability consistent with amlodipine and candesartan poisoning and she was treated with noradrenaline (max 2 µg/kg/h), vasopressin (max 0.04 U/min) and high dose insulin therapy (HIT, max 10 U/kg). Vasopressin and HIT were discontinued 18 hours after arrival, and MB-treatment (2 mg/kg followed by a continuous infusion of 0.5 mg/kg/h) was initiated for treatment-refractory vasodilatory shock. Her blood pressure remained low however, and she developed a non-cardiogenic pulmonary edema necessitating intubation at 22 hours. Around this time the patient rapidly developed spontaneous clonus and muscle rigidity in the lower extremities and jaw, the latter causing her to break a dental bridge while biting down on the endotracheal tube. She became diaphoretic and her body temperature rose to 39 ^{0}C. The symptoms were interpreted as serotonin toxicity precipitated by the use of MB and fentanyl (during intubation) in a patient with a citalopram ingestion (later confirmed by the patient). MB and fentanyl were discontinued and the patient was treated with olanzapine 5 mg intramuscularly. Spontaneous clonus disappeared within minutes and within an hour her muscle rigidity was markedly diminished, her skin dry and her body temperature had dropped to 37.5 °C. A second dose of olanzapine was administered 10 hours after the first, following the recurrence of spontaneous clonus, rigidity and fever, and with a similarly dramatic effect. The patient's hemodynamic and respiratory status gradually improved and she was weaned from vasopressors and ventilatory support during the following 48 hours. There were no further symptoms of serotonin toxicity.
Conclusion: The present case suggests that olanzapine can be a valuable antidote in serotonin toxicity. Traditional treatment options, including heavy sedation and the use of orally administered cyproheptadine, are less than ideal for the unstable intensive care patient and the possible utility of olanzapine in this context warrants close consideration.

269. Non-cardiogenic pulmonary edema in amlodipine poisoning: the lesser evil?

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Objective: Amlodipine lowers vascular resistance by dilating precapillary arterioles, with less effect on the tone of postcapillary venules. This is the physiological background that forms the basis for the non-cardiogenic pulmonary edema that often complicates poisonings with this agent. We report a case that illustrates the dynamic of this pathology.
Case report: A 68-year-old man presented to the hospital 15 hours after ingesting an overdose of amlodipine in a suicide attempt. On arrival his mean arterial blood pressure (MAP) was 55 mmHg, heart rate (HR) 115 bpm, lactate 5.8 mmol/L and creatinine 152 µmol/L. He was treated with 3 L of crystalloids and at 24 hours post-ingestion he became dyspneic with inspiratory crackles. MAP and HR remained unchanged while lactate had normalized. A transthoracic echocardiogram (TTE) showed a hyperdynamic left ventricle. Pulmonary symptoms improved with oxygen and 40 mg of furosemide. He was started on noradrenaline (NA) and further fluids were withheld. At 40 hours the patient was taken to the intensive care unit (ICU) for a persistently low MAP and decreasing urinary output. The NA-dose was escalated from 0.1 to 0.5 µg/kg/min, vasopressin (0.03 U/min) and methylene blue (1 mg/kg as a single bolus) were added and he was given 250 mL of albumin 5%. MAP did not change, the TTE was still hyperdynamic but the patient rapidly desaturated and required emergency intubation for pulmonary edema at 43 hours post-ingestion. After intubation he was maintained on NA and vasopressin and was started on high dose insulin therapy. With these treatments his condition stabilized and gradually improved. He was extubated at 72 hours and discharged from the ICU at 96 hours post-ingestion, in full recovery. An amlodipine blood concentration at 48 hours post ingestion was 0.13 µg/mL.
Conclusion: The present case illustrates how the long duration of vasodilatory symptoms in amlodipine poisoning makes therapeutic restraint difficult, while perhaps all possible interventions risk precipitating pulmonary edema. Vasoconstrictor therapies may cause a greater relative increase in resistance of the less affected post-capillary part of the pulmonary microcirculation. Therapies that increase cardiac output (e.g. fluids) will increase

blood flow over dilated pulmonary arterioles. Both types of intervention thereby increase capillary pressure and the transudation of fluid. However, as the present case illustrates, the complication of pulmonary edema in amlodipine poisoning is manageable and may represent the lesser evil if global perfusion is threatened.

270. Anti-anginal asystole: fatal ranolazine overdose

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Objective: Ranolazine is an antianginal drug, used for chronic angina refractory to first line agents. In oral therapeutic doses, the time to peak plasma concentration is 2-5 hours, with a half-life of 7 hours. High oral doses can produce dizziness, nausea, and vomiting. Ranolazine affects cardiac conduction in multiple ways. It inhibits the late phase of the inward sodium current in myocardial cells. This current exchanges Ca^{2+} via a Na^{+}/Ca^{2+} antiporter, which causes calcium-induced calcium release from the sarcoplasmic reticulum. Thus, ranolazine indirectly acts as a calcium channel blocker. Ranolazine also inhibits the delayed rectifier potassium current (hERG) causing QT prolongation. In cellular models, ranolazine blocks neuronal sodium channels. This may underlie the occurrence of seizures reported in overdose. Few reports of ranolazine overdoses exist, limiting definitive management recommendations. We present a case report of a fatal ranolazine overdose.
Case report: A 67-year-old man with a past medical history of hypertension, coronary artery disease, chronic angina, and schizophrenia presented to the emergency department with a complaint of emesis. He reported ingesting approximately 30 g of extended-release ranolazine several hours prior in a suicide attempt. Physical examination demonstrated an alert male in no acute distress. Vitals signs were: blood pressure 160/87 mmHg; heart rate 72 beats/min; respiratory rate 18 breaths/minute; and pulse oximetry 99% (room air). An electrocardiogram (ECG) showed normal sinus rhythm (73 beats/minute), QT_C 434 ms and QRS 96 ms. Laboratory analysis showed normal electrolytes, renal and hepatic function. Acetaminophen, ethanol, and salicylate concentrations were undetectable. Seven hours after presentation, he developed acute altered mental status with confusion. The ECG showed a first-degree atrioventricular block at 66 beats/minute; PR, 220 ms; QRS 108 ms; and QTC, 450 ms. Nine hours after presentation, three convulsive episodes occurred, each lasting several minutes, before spontaneously resolving. Shortly thereafter, he developed pulseless electrical activity for 20 minutes, followed by ventricular tachycardia, and ultimately asystole. He received defibrillation, continuous cardiopulmonary resuscitation, and advanced cardiac life support, but resuscitation was unsuccessful. An ante-mortem serum ranolazine concentration was 12 mg/L (therapeutic 0.4-6.1 mg/L). Ranolazine is primarily metabolized by CYP3A and CYP2D6. The contributions of his home medications atorvastatin, clonazepam, and clopidogrel (CYP3A substrates) to his clinical picture are unknown.
Conclusion: Based on limited literature reports and this case, ranolazine overdose can cause severe morbidity and delayed mortality, despite initial apparent clinical stability. Patients with ranolazine overdose should be closely monitored for rapid cardiac and neurologic decompensation along with potential consideration for extracorporeal life support (ECLS).

271. Pharmacobezoar and gastric perforation in severe quetiapine intoxication: a case report

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Objective: Modified drug release formulations are invading the market and an exponential increase in their availability is expected in future. In case of recent massive drug ingestion of highly toxic substances, oro-gastric lavage might be considered. If an extended-release (ER) drug is involved, the formation of pharmacobezoar is probable with serious implications on the clinical course of poisoned patients. Kinetic data of ER drugs in severe overdoses are lacking. A case of severe ER-quetiapine intoxication, complicated by gastric pharmacobezoar and associated with gastric perforation, is described.
Case report: A 73-year-old Caucasian female was admitted to the emergency department (ED) after ingestion of 120 pills of ER-quetiapine 400 mg (time of ingestion unknown). At admission, she presented with coma (Glasgow Coma Score (GCS) 3), tachycardia (125 bpm) and hypotension (95/80 mmHg). She was intubated due to her critical condition, and decontaminative gastroscopy was performed. Gastroscopy revealed the presence of multiple pharmacobezoars in the stomach and the esophagus was covered with unmelted drug resides. The bezoars were removed in multiple sessions. Moreover, gastric perforation requiring surgical intervention was documented. Her clinical condition worsened (severe hypotension, QTc 505 ms) and fluids, sympathomimetic drugs and sodium bicarbonate were required. Activated charcoal was not administered because of perforation. A Bogotà bag (temporary abdominal closure) was performed and removed on day 3. Serum quetiapine concentration (reference 100-500 µg/L) was 3857.12 µg/L at ED admission followed by 322.43 µg/L (day 1) and 1193.00 µg/L (day 2). Patient was extubated on day 4.
Conclusion: Materials in ER-drugs are the most probable cause of pharmacobezoar formation, in this case the hydroxypropylmethylcellulose (HPMC) in the ER-quetiapine formulation. Laboratory results confirmed the severity of poisoning and the prolonged absorption when ER-drugs are involved. In case of severe poisoning due to massive ingestion of ER drug formulations, orogastric lavage is ineffective for removing pharmacobezoars and therefore gastroscopy is strongly indicated. In this case gastroscopy was decisive and removed all the gastric contents and permitted identification of an unusual possible complication due to "caustic" effects of bezoars (gastric perforation). This case re-opens the discussion on the role of gastrointestinal decontamination and different procedures to remove material from the stomach.

272. Pharmacobezoar and the holistic approach

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Objective: Potassium poisoning is not very common, and in patients with intact renal function a large amount of potassium has to be taken for the development of life-threatening hyperkalaemia. Certain pharmaceutical products, however, tend to conglomerate in the gastrointestinal tract [1] which affects the risk and severity of poisoning. We report a case of severe poisoning after pharmacobezoar formation.
Case report: A 47-year-old woman with negative past medical history was admitted to the toxicology department after self-administering 50 potassium chloride tablets in a suicide attempt. It was not known whether the tablets were immediate or modified release as the patient had bought them via the Internet and no details were available. The tablets were taken 1.5 hours before her admission. On admission she was alert, vital parameters were stable, and physical examination was unremarkable. Arterial blood gas showed no acid-base disturbance, but moderate hyperkalaemia was detected (6.7 mmol/L). Normal sinus rhythm and peaked T-waves on the precordial leads were demonstrated by electrocardiography (ECG). Gastric decontamination did not retrieve any tablet fragments. Antero-posterior abdominal X-ray revealed a mass in the stomach as a conglomerate of a large number of tablets. Repeated gastric decontamination carried out in Trendelenburg position was not successful. Repeated arterial blood gas analysis showed increased serum potassium concentration, and on the ECG T-waves became progressively worse. In spite of complex conservative therapy (calcium gluconate, sodium bicarbonate, glucose-insulin therapy, polystyrene sulfonate suspension, furosemide) the serum potassium concentration did not decrease. The decision was taken to perform intestinal decontamination and 39 whole intact tablets were removed by urgent upper panendoscopy. This intervention resulted in rapid improvement of the serum potassium concentration.
Conclusion: The potassium tablets in this case were radio-opaque and were seen on abdominal X-ray. In case of a massive overdose the possibility of a pharmacobezoar should always be considered. Potential life-threatening pharmacobezoars can be successfully removed by urgent gastroscopy. Multidisciplinary thinking and management can help in the holistic approach to treatment in these cases.

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273. Intoxication with colchicine: a retrospective study

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Objective: Colchicine is used mainly for the treatment and prevention of gout and for Familial Mediterranean Fever (FMF). It has a narrow therapeutic index, with no clear-cut distinction between non-toxic, toxic, and lethal doses, causing substantial confusion among clinicians. Although colchicine poisoning is sometimes intentional, unintentional toxicity is common and often associated with a poor outcome [1]. We report a case series of colchicine poisoning.
Methods: We retrospectively studied 12 medical records of patients with colchicine poisoning.
Results: Among the 12 cases studied, 5 of them were intentional overdoses, of which 2 patients died. Accidental intoxication occured in 7 cases. Four patients were hospitalized more than 8 hours after drug administration and 8 patients within 8 hours. The average length of hospital stay was 5.5 days, but in the fatal cases it was on average 7 hours longer. There were 6 patients from Yerevan (the capital of Armenia) and 6 from the provinces. Six patients had Familial Mediterranean Fever and the other 6 cases involved 6 children who took another person's drug. The patient's condition in 7 cases was of moderate severity and in 5 cases they were severely affected. The common symptoms were nausea (n = 9), abdominal pain (n = 7), vomiting (n = 4), myalgia (n = 4), rhabdomyolysis (n = 4), headache (n = 3), diarrhea (n = 2), aplastic anemia (n = 2), alopecia (n = 1) and seizures (n = 1). In mild cases, there were no biochemical or hematological changes but in moderate-to-severe cases there was hyponatremia, elevated creatine kinase (CK), leukopenia, pancytopenia, coagulopathies and elevated levels of liver and kidney markers.
Conclusion: Armenia is an endemic region for Familial Mediterranean Fever and it is important to know the signs and symptoms of the disease and also the signs of colchicine intoxication. We conclude that the most common symptoms are gastrointestinal manifestations. Early admission, diagnosis and treatment is associated with less risk of serious complications. There is a necessity to increase awareness in patients with FMF to avoid inadvertent uses of high doses of colchicine.

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274. Use of laboratory tests for identifying patients at risk of an incomplete response to the recommended dose of idarucizumab

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Objective: Increasing reports of incomplete responses to idarucizumab for immediate reversal of dabigatran-induced anticoagulation prompts consideration of circumstances when the recommended idarucizumab dose will be inadequate. Laboratory tests and thresholds indicating this risk are desired.
Methods: Systematic literature review conducted for publications describing an incomplete response to the recommended 5 g idarucizumab, in particular those requiring additional idarucizumab. An incomplete response was defined as persistent, or a significant rebound, in dabigatran concentrations and/or coagulopathy to levels sufficient to induce clinically significant anticoagulation. Dabigatran concentrations 75-240 ng/mL were considered therapeutic with routine use. The impact of threshold dabigatran concentrations on routine coagulation tests was also considered.
Results: Dabigatran concentrations exceeding 20 ng/mL are associated with recurrent or continued bleeding. In patients who

received idarucizumab, dabigatran concentrations <200 ng/mL usually had a complete response, 200-500 ng/mL was associated with an incomplete response, and >500 ng/mL were at the highest risk of an incomplete response, particularly when >1000 ng/mL. Patients with acute and chronic kidney dysfunction are at increased risk due to higher dabigatran exposures and pharmacokinetic differences between these drugs. These observations largely apply to patients on chronic dabigatran therapy; on the basis of a couple of cases they do not apply in acute self-poisoning. These thresholds cannot be used to evaluate the timing and extent of the rebound and they do not apply to all cases, reflecting clinical heterogeneity. The dilute thrombin time (dTT) is directly proportional to the concentration of dabigatran but its sensitivity is reduced at dabigatran concentrations <50 ng/mL so is unreliable for excluding dabigatran. Dabigatran and aPTT have a curvilinear relationship, but a normal aPTT excludes dabigatran and >90-100 s corresponds to dabigatran concentration >500 ng/mL. Dabigatran and INR have a linear relationship, but INR is normal until dabigatran >62 ng/mL and INR 2.0 correlates approximately to dabigatran 400 ng/mL.

Conclusion: An incomplete response to idarucizumab occurs when the body burden of dabigatran exceeds the binding capacity of idarucizumab. In the absence of dTT or a specific dabigatran assay, aPTT can be used to rule out significant dabigatran concentrations both pre- or post-idarucizumab, and both INR and aPTT can identify those with a dabigatran concentration that will not be fully reversed by a standard dose of idarucizumab. Coagulation studies and/or dabigatran concentrations should be tested every 6 hours for a minimum of 24 hours after idarucizumab to identify an incomplete response.

275. Physostigmine and cyclobenzaprine: summary of safety and efficacy in 30 patients

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Objective: To describe the incidence of adverse effects and efficacy of physostigmine for reversal of anticholinergic symptoms related to cyclobenzaprine intoxication.

Methods: Retrospective review of medical records for a subset of 30 patients who ingested cyclobenzaprine out of all patients who received physostigmine for anticholinergic toxicity at an academic 850-bed, tertiary-care hospital from March 2011 through July 2016.

Results: Out of 227 patients that received physostigmine during this 5-year period 30 (13.2%) were identified to have ingested cyclobenzaprine. Three (10%) cyclobenzaprine patients ingested additional anticholinergic agents. Overall, 28 were intentional self-poisonings, one (a 4 year-old) unintentional, and one was an adverse effect of therapeutic use. Mean age was 35.6 years (range 4-64, 6 were less than <18 years-old) and 16 (53.3%) were female. While drug testing for causative agents was infrequently performed 7 (23%) had cyclobenzaprine identified using an expanded qualitative "panel" that included pharmaceutical agents. Cyclobenzaprine was identified in the remaining 23 (77%) of patients by history and corroborating information. A total of 45 doses of physostigmine were administered in these 30 patients. The 2 mg dose was most common and was used in 22/30 (73%) of first doses. Ten patients received a second physostigmine dose (8/10 were 2 mg) a mean 6.2 hours (range 0.1-23 hours) after the first dose and five received a third dose (3/5 were 2 mg) a mean 20 hours (range 2-54) after the second dose. The first physostigmine dose was effective in reversing coma in 10/15 (66%) and agitation or delirium in 14/23 (61%). Coma, agitation, or delirium recurred within 60 minutes following initial improvement in 7/10 (70%), 8/10 (80%), and 11/12 (92%), respectively. Electrocardiogram results were documented in 22 patients; mean QRS 90 ms (range 74-116) and QTc 445 ms (range 360-507). Concomitant administration of benzodiazepines and physostigmine occurred in 11 patients and 5 received multiple benzodiazepine doses. There were no episodes of seizures, vomiting, bradycardia, or other cardiac dysrhythmias in patients that received physostigmine for cyclobenzaprine toxicity.

Conclusion: Physostigmine was safe and effective in reversing anticholinergic toxicity from cyclobenzaprine. While most patients (70-92%) that responded to physostigmine had recurrence of coma, agitation, or delirium within 60 minutes, physostigmine was only repeated in ten patients a mean of 6.2 hours later. Whether additional benefit can be gained with more frequent dosing, or use beyond diagnostic purposes for some patients, warrants further study.

276. Post-overdose cognitive function

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Objective: Patients with sedative overdose may have residual cognitive impairment even when medically cleared. Impairment could affect performance of high risk activities that require coordination and attention, including operating machinery or driving [1]. We determine if there is a difference in subclinical cognitive function in patients that overdose on central nervous system (CNS) depressant (sedative) and non-depressant drugs.

Methods: A prospective, non-blinded observational study was conducted at Prince of Wales Hospital (Sydney, Australia). Cognitive function was assessed using the Trail Making Test (TMT), a brief, two-part bedside test. The more complex part B assesses task switching and executive function, and was correlated with driving ability [2]. Patients completed TMT at medical clearance, were ≥16 years old, spoke English, and had no previous neurological injury. Patients were compared using Mann-Whitney U tests and ANOVA.

Results: Of 89 patients, 59 (66.3%) took sedative drugs. Nonsedative drug users were younger, but other demographic characteristics were similar (Table 1). Benzodiazepines and antipsychotics were the commonest drug groups. Median TMT-A times were 35.9 s (IQR: 27.0-41.5) and 40.4s (IQR: 30.1-51.0) for non-sedative and sedative drugs respectively ($p = 0.1$). Median TMT-B times were 79.6s (IQR: 67.0-97.1) and 95 s (IQR: 80.0-158.0) for non-sedative and sedative drugs respectively ($p = 0.005$). Between sedative types, ANOVA indicated no difference in TMT-A ($p = 0.61$) and TMT-B ($p = 0.46$) times.

Conclusion: Patients admitted to hospital following CNS depressant drug overdoses may have significant cognitive deficits at the time of medical clearance when compared to CNS non-depressant overdoses. Risk of harm may be mitigated through avoidance of higher risk activities such as driving.

Table 1. Clinical characteristics and results of cognitive function tests (Trail Making Test) of patients with CNS depressant and non-depressant drug overdose.

	Sedative overdose (59 patients)	Non-sedative overdose (30 patients)	P value
Mean age in years	35.7	26.0	0.002
Female (%)	27 (45.8)	19 (63.3)	0.18
Concurrent alcohol consumption* (%)	30 (56.6)	12 (42.9)	0.25
Median TMT-A time in seconds (IQR, Range)	35.9 (27.0-41.5, 21.0-74.0)	40.4 (30.1-51.0, 17.0-123.2)	0.10
Median TMT-B time in seconds (IQR, Range)	95.0 (80.0-158.0, 51.5-300.0)	79.6 (67.0-97.1, 33.0-300)	0.005
Most common drug type (number of patients)	Benzodiazepine (31)	Paracetamol (6), SSRI (6)	–
Number of ICU admissions	4	1	0.66
Median length of ICU admission in days (Range)	2 (1-5)	1	–
Median length of stay in days (IQR, Range)	1 (0-1, 0-5)	1 (0-1, 0-1)	0.99

TMT-A: Trail Making Test part A; TMT-B: Trail Making Test part B; IQR: interquartile range. *8 patients did not provide data for alcohol consumption.

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277. Toxicoepidemiology: assessment of conventional and traditional management of scorpion sting in Beitbridge district, Zimbabwe

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Objective: The aim was to describe the epidemiology of scorpion sting admissions in Beitbridge district, Zimbabwe and to investigate the ethno-medicines used in the traditional management of scorpion stings.

Methods: A retrospective and cross-sectional study was used. A preformatted data form was used to review and enter all scorpion sting cases at Beitbridge District Hospital from January 2015 to December 2017, inclusive. Oral interviews were also carried out in Chituripasi village in the district using an interview guide. Data analysis was done using Microsoft Excel 2013.

Results: A total of 210 cases were obtained for the three year study period. The male to female ratio was 1:1.3. The 20-29 age group had the highest number of envenomation cases. Hydrocortisone, promethazine, subcutaneous lidocaine, 0.5 mL Antitetanus Toxoid and analgesics (paracetamol, ibuprofen and indometacin) were the drugs administered to patients. No patient received scorpion antivenin. Most envenomation cases occurred in the month of December (24%) with the lowest reported in August (0.04%). The prevalence of use of traditional medicines was found to be 4 (10%) in the 60-69 year old population ($p = 0.049$) and was shown to increase with age. Out of 40 participants, 10 (25%) acknowledged to have used traditional medicines for scorpion sting. The participants reported using Forest bitter berry (*Solanum xanthocarpum*), false daisy (*Eclipta prostata*), Castor plant (*Ricinus communis*) and Lucky bean creeper (*Abrus precatorius*).

Conclusion: Scorpion sting cases were higher in urban Beitbridge compared to rural areas and females were most commonly affected. No mortality was recorded at the hospital due to scorpion sting over the three year study period. Ethno-medicine is still practiced in Beitbridge district but on a small scale and is most prevalent in older patients.

278. The changing pattern of treatment for latrodectism over time in a toxicology unit: red-back spider antivenom or standard analgesic therapy: nothing to RAVE about

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Objective: Red-back spider (RBS) envenoming (latrodectism) can result in local, regional or generalised pain and autonomic overactivity. In 2014, the Australian RAVE-2 study found intravenous RBS-antivenom (RBSAV) was no more effective than placebo in improving pain from envenoming [1]. Anecdotally, RBSAV use appears to have decreased since this study. We aimed to assess the change in frequency of antivenom use, and responses to various treatments for latrodectism in our toxicology unit.

Methods: Retrospective observational study of RBS bite referrals, October 2009 to June 2019. Data extracted included demographics, pain severity (mild 1-3/10, moderate 4-6/10, severe 7+/10), treatment (oral or intravenous analgesia, RBSAV; IM or IV), response to treatment (no response or partial/complete resolution of pain), representation rate, adverse events (allergic reactions, serum sickness), antivenom prescribing frequency over time. Response to treatment was compared between groups using Fisher's exact test.

Results: There were 252 presentations with latrodectism. Median age 36 (range: 2-91) years, 46% female. Pain was mild in 39%, moderate 19%, and severe 38%. Initial pain not recorded in 4.4%. Patients with mild or no initial pain score were excluded from further analysis, leaving 142 cases. RBSAV was administered as initial treatment to 35% ($n = 50$), and standard analgesia in 65% ($n = 92$). RBSAV was administered IM (43%), IV (47%), and IV/IM (10%). Median dose was one vial (range 1-4). Those administered only analgesia received a combination of paracetamol, ibuprofen and oral opioids (52%), paracetamol and ibuprofen (34%), or combination paracetamol, ibuprofen, oral and parenteral opioids (7.5%). In patients receiving antivenom, 91% reported a partial or complete reduction in pain and were discharged home and 94% of patients receiving analgesics had a partial or complete response and were discharged ($p = 0.7$, OR:0.7 [95% CI:0.16-2.8]). There was no difference in response to treatment between the groups. Ongoing pain resulted in re-presentation in 6% ($n = 3$) after RBSAV and 14% ($n = 13$) after analgesic therapy ($p = 0.1$, OR:2.6 [95% CI:0.7-9.5]). Notably, 82% of patients received antivenom from 2010 to 2013. There were three instances of serum sickness and one allergic reaction (rash) to antivenom.

Conclusion: RBSAV use declined over time in our unit from 2014, most likely attributable to change in practice after the RAVE-2 study. Comparison of response to treatment in patients with moderate to severe pain did not show a difference in pain

reduction or re-presentation rate between RBSAV and analgesia treatment.

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279. Ciguatoxin concentrations in fish may be unreliable in ciguatera fish poisoning toxicovigilance studies

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Objective: Although under reported, ciguatera fish poisoning (CFP) is the most common form of non-bacterial food-poisoning from fish [1]. It is essential that it be detected for public health control of seafood toxin diseases in humans. Ciguatera toxin detection is part of toxicovigilance studies by public health units. We report a family of three with ciguatera fish poisoning and laboratory analysis of a fish sample.
Case series: Two females, 48 and 60-years-old, and a male, 53-years-old, of the same family, presented to a tertiary Emergency Department in Western Sydney Australia, with symptoms of CFP. They had bought a large Sweetlip Emperor reef fish (*Lethrinus miniatus*) from a local seafood store. It was refrigerated overnight, cooked and consumed the following day. Three hours after consumption, all patients developed nausea, vomiting, abdominal cramps, diarrhoea and pruritus. They described myalgias, circumoral and extremity paraesthesias. There was no thermoalgesia. Based on these neurological and gastrointestinal symptoms, a clinical diagnosis of CFP was made [3]. Public health was notified, and the supply of the fish was traced back to the fish markets from which the fish were distributed throughout the state. Multiple other cases of CFP were detected in New South Wales that week, linked to the same supplier. A cooked sample of fish was sent for laboratory analysis. Ciguatoxin was not detected.
Conclusion: Ciguatoxin concentrations in samples may be underestimated due to matrix suppression from compounds present in fish tissue [2]. Multiple ciguatoxins have been identified [3]. The complexity and variability of ciguatoxins poses difficulty in developing reliable methods to diagnose CFP based on ciguatoxin concentrations with specificity and sensitivity [4]. CFP diagnosis is based on a history of consuming reef fish, time course of symptoms, and exclusion of other causes. Ciguatoxin concentrations may be unreliable in diagnosing CFP to aid toxicovigilance studies.

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280. A serious viper bite in a pregnancy

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Objective: Snake bite envenomation in pregnancy is unusual. Antivenom is the mainstay of therapy, but its effects on the fetus are not well-known. We describe the clinical course of a serious viper envenomation (Grade Severity Score, GSS 2) in a pregnant woman treated with viper venom antitoxin.
Case report: A 37-year-old 31 week pregnant woman was bitten by a snake on the right ankle. The snake was not captured or photographed, but was likely to be *Vipera aspis.'* The patient was quickly referred to Grosseto Hospital, where she was treated with antibiotics, corticosteroids and compressive bandage, due to mild local sign (GSS 1). Following a multi-disciplinary consultation, considering impending fetal distress and the possibility of a rescue surgical delivery, she was transferred to Siena University Hospital, where a Neonatal Intensive Care Unit is available. She had Glasgow Coma Score (GCS) 15 and many episodes of vomiting and diarrhea, dehydration with mild lactic acidosis, bilateral ptosis, photophobia, limb paresthesia, painful edema of the leg to the knee, body temperature 38 °C (GSS 2). The Florence Poison Centre contacted four hours after the event suggested and provided two vials of antitoxin. After pre-treatment with corticosteroids and antihistamine, the patient received the antitoxin eight hours after the snake bite, without any adverse effect. A cardiotocography (CTG) showed mild maternal uterine contractile activity treated with tocolytics. Fetal heart rate was regular. Maternal inflammatory markers and D-dimer were rising thus low molecular weight heparin was administered. The day after, the edema had extended to the right hip and to the vulvae. Arterial-venous Doppler excluded thrombosis and D-dimer values started to decrease. CTG and ultrasound showed no residual contractile uterine activity as well as a vital and reactive fetus. On day 2, due to acute anemia (Hb 7.4 g/dL) the patient was transfused with two units of concentrated red blood cells, meanwhile D-dimer values were further decreasing. On day 3 hematuria, cough, dyspnea, and hypoxemia were reported. Bilateral pleural effusion and bi-basilar atelectasis were present on chest X-ray and treated with antibiotics, corticosteroids and oxygen. CTG and ultrasound showed no alterations. The right leg and the vulvar edema resolved on day 8 and 11, respectively. The patient was discharged on day 18.
Conclusion: In the rare case of GSS 2 viper envenomation in pregnancy, beside supportive treatment, specific antitoxin treatment was effective and safe both for the mother and the fetus. Fetal monitoring is also suggested in these cases.

281. Spider bites in France: a retrospective study using the French Poison Control Centers Network from 2007 to 2017

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Objective: Spiders are usually feared and are often incriminated in cases of a skin eruption. The aim was to describe the last 11 years of spider bite calls to the French Poison Control Centers network (PCCn).
Methods: A retrospective study of spider bite calls to the French PCCn from 2007 to 2017 describing the spatial and temporal distribution of the alleged bites, species identification, sociodemographics and symptoms.
Results: In 11 years, 1136 cases involving a spider bite were recorded, representing an average of 103.3 cases per year; 47% of cases (n = 534) occurred during summer. The Mediterranean region was the first area represented with 16.3 cases per 100,000 inhabitants in Corsica and 4.5 cases per 100,000 in Provence-Alpes-Côte d'Azur. Bites usually involved adults (65.4% between 21 and 60 years); the sex ratio (M/F) was 0.92. The relationship between spider bites was assessed as likely or very likely in 45% of cases, however, spider identification was rated as good in only 28.2% of cases, with a photograph of the animal examined by an expert or a toxicologist. The identified spiders mainly belonged to 3 genera: *Loxosceles* (n = 43), *Latrodectus* (38 cases), and *Cheiracanthium* (n = 31). Pet mygales were involved in 17 cases. The other genera identified were *Steatoda* (n = 2), *Tegenaria* (n = 6), and *Araneus* (n = 2). According to the Poisoning Severity Score (PSS) [1], the severity of the cases was as follows: PSS0 3%, PSS1 78%, PSS2 17% and PSS3 2%. While the majority of patients had mild localized skin symptoms at the bite site (74.7%), local necrosis or skin infection was reported in 45 and 73 patients, respectively. Neurovegetative disorders (headache, dizziness, loss of conscious, diaphoresis, chills) were described in 9.6% of cases, digestive signs in 2.4% of cases, neuromuscular signs in 5.1% of cases and cardiovascular signs in 29 patients. For 22.6% of patients, medical consultation was provided. Antibiotics were prescribed in 14.8% of cases, and analgesics in 7.1% of cases. Of the 45 reported cases of necrosis, 35.6% were surgically treated. A skin graft was required for one case. There were no deaths, however, four patients showed persistent local signs 3 weeks after the bite.
Conclusion: Although symptoms are frequent, spider bites only cause severe disorders for a very small number of species. The causality of symptoms related to the exposure, precise and quick identification of the cause are difficult to establish, and most of the time are uncertain. In our country, spiders appeared to be less dangerous than many other less scary animals.

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282. Prolonged morbidity after fish stings: a callback survey at the Norwegian Poison Information Centre (NPIC)

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Objective: Excruciating pain after fish stings is well documented. Long-lasting symptoms are known to occur infrequently. Numerous calls to the NPIC concerning lasting pain after fish stings have made us question whether the frequency of prolonged morbidity may be underreported. We therefore conducted a callback survey to learn more about these envenomations, focusing particularly on prolonged symptoms.
Methods: The first line responders at the NPIC asked for consent to callback all exposed patients after fish stings, between May and September 2019. One person carried out all callbacks to ensure consistency. Callbacks were made from three weeks post-exposure. In some cases with prolonged symptoms, a second interview was conducted.
Results: There were 35 calls to the poison centre regarding fish stings in the survey period. Due to lack of consent, unreachable patients and uncertain exposures, we included 19 patients. Twelve were stung by the greater weever (*Trachinus draco*), two by rose fish (*Sebastes* sp.), two spiny dogfish (*Squalus acanthias*), one ray (Batoidea), one rabbit fish (*Chimaera monstrosa*) and one by an unknown fish. The patients, 15 men and 4 women, all adults, and were stung on the finger or the hand. Three patients did not immerse the exposed area in hot water as recommended. Pain was the predominant symptom reported. The patients were all asked to grade their initial pain on a scale from 1 to 10. One patient graded it as mild pain (between 1-3), five as moderate (between 4-6) and 13 as severe (between 7-10). Thirteen patients had local swelling. Three patients experienced nausea, dizziness and profuse sweating, linked to severe initial pain. No one experienced severe acute systemic symptoms. Infection occurred in one patient suffering from a residual spine that was surgically removed after a few days. Three patients had no symptoms after 24 hours, four had symptoms lasting 1 to 7 days, and eleven patients experienced symptoms longer than 3 weeks after exposure, five of which had pronounced morbidity (pain, intermittent joint complaints, reduced mobility, hyperesthesia). One patient experienced lasting generalized neuropathy, possibly linked to the exposure.
Conclusion: The prevalence of long-lasting symptoms was higher than anticipated. The severity of the initial pain did not seem to be a good predictor for the duration of symptoms, but our survey is too small to make firm conclusions. We will now inform the patients of the risk of protracted clinical symptoms during the initial contact with the NPIC.

283. Recurrent thrombocytopenia after Italian viper bite: a case report

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Objective: Thrombocytopenia and coagulopathies are well known effects of viper bite envenomation. Several mechanisms can alter platelet count. A reduction may be due to consumption coagulopathies and degradation mediated by serine proteinases and phospholipases A2 [1]. Profound thrombocytopenia has been described in two patients after *Vipera ammodytes ammodytes* bite [2]. We report a case of recurrent thrombocytopenia after envenomation, effectively treated with antivenom, with transient antiplatelet antibodies detection.
Case report: A 42-year-old man was admitted in the emergency department three hours after a viper bite, with only mild local symptoms. Blood sample showed a tendency to thrombocytopenia. During the observation, he developed local lymphedema, D-dimer increase and a constant platelet count reduction. Forty hours after the bite, platelet count dropped to 4000 with no bleeding signs, so he received antivenom (ViperaTAb®, 2 vials). Three hours later, thrombocytopenia transiently improved (34000) to decline again after few hours. Twelve hours after the first treatment, a second dose of antivenom was administered, as platelet count was again 5000. Again, an initial increase in the number of platelets was followed by a reduction. Five days after the bite, the platelet count fluctuated between 4000 and 5000 elements. Steroid and immunoglobulin therapy was started for thrombocytopenia with a suspected autoimmune origin, which was confirmed by laboratory detection of both direct and indirect antiplatelet antibodies. In the following days, the platelet count gradually improved and the patient was discharged after ten days of hospitalization, with 126000 platelets. A reassessment 7 days after discharge showed no local symptoms, a platelet count of 199000 and negative for antiplatelet antibodies.
Conclusion: Variable degrees of thrombocytopenia have been described after nose-horned viper bites [2]. In our clinical case, based on geographical localization, we also can hypothesize the involvement of *Vipera ammodytes ammodytes*. A recurrent thrombocytopenia was noted despite effective repeated antivenom treatments. Moreover, antiplatelet antibodies were observed and hematological parameters improved after 10 days of steroid and immunoglobulin treatment. We suggest the utility of monitoring coagulation parameters for at least 10 days after severe envenomation and, in case of recurrent thrombocytopenia, investigate viper venom-induced immune thrombocytopenia.

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284. *Latrodectus tredecimguttatus* poisoning: a case report treated with antidote

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Objective: Latrodectism is a very rare, but potentially lethal, clinical syndrome caused by spiders of the genus *Latrodectus* [1]. In Italy, following the bite of the female of malmignatta (*Latrodectus tredecimguttatus)*, the α-latrotoxin in the venom causes depletion of acetylcholine at motor nerve endings and release of catecholamines at adrenergic nerve endings [2]. We describe the first use in Italy of *Latrodectus* antidote in a patient with severe malmignatta poisoning.
Case report: The patient was working in his garden when he felt a sort of sting on the lower leg associated with an intense burning sensation. An hour later he developed agitation, dyspnea, hoarseness, sweating and abdominal pain. In the emergency room vital signs showed a hypertensive crisis, tachycardia, and peripheral oxygen desaturation. Electrocardiogram (ECG) was normal and blood gases showed mixed acid-base disorder. Blood tests showed leukocytosis with neutrophilia, high levels of myoglobin, with normal coagulation and plasma cholinesterase. Neck, thorax and abdomen computerised tomography (CT) scans with and without contrast medium were negative. Four hours after admission the hypertension worsened with a board-like rigid abdomen and onset of fasciculations, tremors, miosis and intense sweating. The definitive diagnosis of poisoning by *Latrodectus tredecimguttatus* was based on the clinical picture. Within a short time Specific Anti-*Latrodectus* Serum® was provided by our Poison Control Centre (PCC) and administered. A marked improvement in the symptomatology was noted after 30 minutes, and 1 hour later all symptoms were under control. The patient was discharged after 2 days.
Conclusion: Latrodectism is a challenging diagnosis. Following the suspicion, the first-line doctor is invited to discuss the case with a PCC physician, in order to confirm or exclude the diagnosis and implement all therapeutic measures. In our case, considering the worsening of the patient's clinical condition, the decision was made to administer Specific Anti-*Latrodectus* Serum®. Rapid treatment with improvement of the patient's condition was guaranteed by prompt supply of the antidote stored at our PCC. This is, to our knowledge, the first use of the specific antidote against *Latrodectus* in Italy, and confirms its effectiveness in counteracting the symptoms caused by the Mediterranean Black Widow spider.

References

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285. Prolonged neurological effects after delayed antivenin administration

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Objective: The timing and specific indications for administration of antivenin after a contact with a *Micrurus fulvius* (eastern coral snake) varies amongst toxicologists. Bites from *Micrurus* species produce significant neurologic deficits that may be delayed 12-18 hours [1], and are thought to most likely be due to the effects of the phospholipase A_2 component of the venom [2]. Once

there is onset of the descending bulbar paralysis, antivenin administration may not fully resolve those effects. We report a case of prolonged ptosis and disconjugate gaze from a *M. fulvius* bite associated with a delay in antivenin administration despite initial systemic effects.
Case report: A 10-year-old male presented to a healthcare facility 1.5 hours after reporting 2 bites to the palm of his hand from a coral snake. A photo of the snake was produced. He reported a syncopal episode and several episodes of nausea and vomiting during his trip to the emergency department. He was initially not treated with antivenin due to the absence of skin changes or a history of the snake latching onto the patient. After developing shooting pain associated with continued retching, he was administered 1 vial of antivenin 9 hours post-envenomation. Another 4 vials were given at hour 12. At 15.5 hours, he developed ptosis and diplopia and another 4 vials were completed at 22 hours post-bite. He received an additional 4 vials of antivenin due to persistent symptoms. A total of 13 vials of antivenin were given. He was discharged on day 4, with persistent ptosis and disconjugate gaze. Although his ptosis resolved after a month, his visual disturbances took 7 months to normalize which greatly affected his daily activities.
Conclusion: Administration of *Micrurus fulvius* antivenin should be started without delay after a credible report of a bite, especially when systemic effects are present. Previous myths regarding envenomation circumstances and need for neurologic findings prior to antivenin administration should be discounted. Delay in antivenin administration may allow neurologic symptoms to develop that may be prolonged or permanent.

References

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286. Cardiovascular complications following ciguatera fish poisoning in the French West Indies: a case series

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Objective: Ciguatera is one of the most common cases of marine poisoning associated with fish consumption in the world. The incidence of this intoxication is largely unreported. In Martinique, the incidence of this intoxication seems to be increasing. During the last 3 years, numerous cases of large collective poisonings have been reported in Martinique, especially during summer. The spectrum of clinical manifestations is large including gastrointestinal, neurological and cardiovascular symptoms. Ciguatoxin, the toxin responsible for ciguatera fish poisoning is considered as a sodium channel agonist with cholinergic and adrenergic activity. It is rarely fatal and management of poisoned patients is essentially based on supportive care. The objective of this study was to describe the clinical characteristics and complications of ciguatera poisoning in Martinique, focusing on the cardiovascular effects.
Methods: Observational, retrospective, single-center study covering a 6-year period October 2012 to September 2018, including all patients admitted to the Emergency Department of the University Hospital of Martinique (CHU), and all patients who were reported to the Regional Health Agency (ARS) for ciguatera intoxication.
Results: Overall 149 patients with ciguatera poisoning were included. The incidence rate found was to be 0.67 cases per 10,000 patient-years in Martinique over the period. About 90% of patients had gastrointestinal symptoms such as nausea, vomiting, diarrhea, or abdominal pain; 83% neurological disorders and 42% cardiovascular symptoms including, bradycardia, hypotension and interventricular block. Ingestion of Carangue fish was related to a major risk of chronic signs.
Conclusion: The incidence of ciguatera in Martinique is increasing, with 0.67 cases/10,000 patient-years. The clinical presentation is defined mainly by digestive signs, followed by peripheral neurological disorders and cardiovascular symptoms. Ciguatera fish poisoning in Martinique presents a similar clinical presentation to that of the other Caribbean Islands, and acute ciguatera poisoning is responsible for significant cardiovascular complications. There is no specific treatment. Physicians should be aware of the potential cardiovascular risk of ciguatera poisoning.

Reference

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287. Epidemiology of bites by indigenous venomous snakes in Switzerland reported to Tox Info Suisse over a 22 year period

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Objective: Switzerland is home to two indigenous venomous snakes with overlapping habitats, the asp (*Vipera aspis*) and the common adder (*Vipera berus*). Bites by both vipers cause local effects such as pain and edema, however, victims may also exhibit systemic envenoming, e.g. hematotoxic and/or neurotoxic symptoms, as well as anaphylaxis.
Methods: Analysis of all calls concerning snakebites recorded at the Swiss National Poisons Information Centre, 1997-2018, including all cases with identification by a herpetologist, and/or with symptoms and circumstances of the exposure compatible with a potential snakebite. Exclusion criteria comprised non-venomous snakes, exotic snakes, or calls from abroad.
Results: During the study period, 1364 calls related to snakebites were recorded; the majority (751, 55%) were attributed to indigenous snakes, and 466 (62%) attributed to vipers. Follow-up information was available for 243 (52%) patients, with good causality (probable) for 219 (90%) patients. *Vipera aspis* was identified in 77 cases (35%), *Vipera berus* in 54 (25%) and in 88 (40%) the snake was not specified. The majority of cases (155, 70%)

involved adults (male 109, female 46, median age 43, range 16-90 years), with 64 children (male 47, female 16, unknown gender 1, median age 11, range 1.3-15.9 years). Nearly two thirds of the bites occurred in the summer, with peaks in the hot months of June (40, 18%), July (51, 23%), and August (43, 19%). Most annual bites (16 versus an average of 10 bites per year) were recorded in the year 2016, which was among the ten warmest years in Switzerland since national climate observations began in 1864, with a record-breaking warm winter and dry summer period. In the majority of patients the clinical course was mild (94, 43%) or moderate (80, 36%); a lower proportion were asymptomatic (17, 8%) or exhibited severe symptoms (28, 13%). There were no fatalities. Antivenom was administered in 10% (22 patients: 14 with moderate and 8 with severe symptoms) with good resolution of symptoms, while the remainder were treated symptomatically. The mean duration of hospitalization was 2 days (0-12 days), and was dependent on severity (with severe symptoms the mean duration of hospitalization was 4 days).

Conclusion: Snakebites in Switzerland can result in severe symptoms, sometimes necessitating antivenom treatment. The risk of bites is higher in the warmer months.

288. Bites by *Cheiracanthium punctorium* in France: a case series

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Objective: The yellow sac spider *Cheiracanthium punctorium* is characterized by a yellow green abdomen with a green dorsal mark. The orange carapace bears long green legs and prominent chelicerae, and the spider is very easy to identify. The venom contains several proteolytic enzymes and a unique polypeptide toxin, CpTx1, which possesses insecticidal, haemolytic, cytotoxic and membrane-damaging activities [1]. The spiders bite defensively especially during the summer when females protect their eggs after mating. We describe bites by *Cheiracanthium punctorium* in France, examining the population concerned, clinical symptoms and severity.

Case series: Over a 10-year period (2009 to 18 September 2019) *Cheiracanthium punctorium* bites recorded by French Poison Control Centres were collected. A total of 36 cases were recorded with females 58% (n = 21), males 42% (n = 15) with median age 37 years and mean age 34 years. Of these cases 71% of bites occurred in southern France and in most cases (86%) during the summer (July to September). Cases have increased over the past few years with 13 cases between 2009 and 2013 and 23 cases between 2014 and 2019. All the patients had 2 bite marks, with local transient cutaneous effects around the bite, and very intense pain, which was difficult to relieve with painkillers and required medical help. In addition 6% of patients (n = 8) had paresthesia and general symptoms such as nausea, vomiting, or abdominal pain (11%, n = 4), hyperthermia (5%, n = 2), and headache (3%, n = 1) were also reported. Only one patient had necrosis. The Poisoning Severity Score was 2 for 69% of cases (n = 25) due to intense pain, and 1 for 31% of cases (n = 11). Overall 70% of patients (n = 25) recovered in 48 hours without ulceration.

Conclusion: *Cheiracanthium punctorium* bites seem to be rare events, but in fact are not uncommon, and they appear to be increasing, possibly due to global warming. This spider species must be known not only by toxicologists but also by emergency doctors.

Reference

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289. An analysis of envenoming features in adder bite cases referred to the UK National Poisons Information Service (NPIS)

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Objective: The adder (*Vipera berus*) is the UK's only native venomous snake. Health professionals contact the UK National Poisons Information Service (NPIS) for advice regarding the management of adder envenoming, in particular the administration of antivenom. We aimed to identify the severity of envenoming and the range of clinical features of cases referred.

Methods: We analysed prospective data collected over a 4-year period (2016-2019) on all NPIS telephone enquiries involving adder bites for which antivenom was given. Data were analysed with respect to clinical features of envenoming and the number of doses of antivenom required.

Results: Over the study period, the NPIS received 131 telephone enquiries (approximately 33 calls per year) regarding adder envenoming which required administration of antivenom. Most patients (119; 90.8%) experienced marked swelling beyond the next major joint from the bite site (one of the main criteria for administration of antivenom). Systemic effects, including abdominal pain and vomiting (29; 22.1%), hypotension (20; 15.3%) and anaphylaxis-like reactions (16; 12.2%), also occurred frequently. Other criteria for antivenom were less frequently observed (raised D-dimer n = 14, 10.7%, ECG abnormalities n = 8, 6.1%, metabolic acidosis n = 5, 3.8%, elevated creatine kinase n = 4, 3.1% and leucocytosis n = 1, 0.8%). Some patients developed multiple features of envenoming which contributed to their overall clinical picture. Most patients experienced rapid cessation of systemic envenoming or progression after a single dose of antivenom (92; 70.2%). Thirty-five patients (26.7%) received two doses of antivenom, and four (3.1%) required three doses.

Conclusion: The UK NPIS receives approximately 33 enquiries per year concerning envenomed patients requiring antivenom following an adder bite. The most frequently observed clinical features are marked local swelling with a lower incidence of systemic features including anaphylaxis-like reactions, hypotension, and abdominal pain and vomiting. While the majority of features resolved following a single dose of antivenom, around 30% received more than one dose.

290. Kambô: a healing potion or a poisonous toxin?

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Objective: Kambô is a secretion extracted from the Giant Amazonian Leaf Frog (*Phyllomedusa bicolor*) reported to contain the natural opioid peptides dermorphin and deltorphin. It is used in traditional South American healing rituals, through application to open wounds, for its alleged strengthening and spiritual qualities. It is becoming increasingly popular worldwide as a therapy for pain, depression and substance misuse. Following recent reports of toxicity including associated fatalities [1], our aim was to analyse enquiries to the UK National Poisons Information Service (NPIS) regarding kambô.
Methods: We conducted a retrospective analysis of enquiries to the NPIS regarding kambô. Cases were identified from the UK Poisons Information Database (UKPID) using the search terms, "Kambo Frog Toxin (*Phyllomedusa bicolor*)" and "Frog nk". All cases recorded as "Frog nk" were individually assessed to identify those relating specifically to kambô.
Results: The NPIS received 9 enquiries relating to 6 patients. Five patients were male and the average age was 39 years (range 23-55; 1 unknown). A range of clinical features were reported (Table 1). Toxicity was determined to be moderate or severe (PSS2 or 3) in 4/6 cases (66%). One patient developed severe symptoms (PSS 3) including a respiratory arrest, however, dihydrocodeine was co-ingested and this may have contributed to the clinical picture. There were no fatalities.
Conclusion: Exposure to kambô is rare in the UK but it is an emerging cause of poisoning worldwide with increasing cases reported outside traditional South American communities. While it is reported to contain opioid peptides, many of the clinical features are not consistent with an opioid toxidrome. Further studies are needed to improve understanding of the toxicity associated with this traditional practice.

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291. Viper bite neurotoxicity: two pediatric cases in central Italy

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Objective: In Italy envenomation from a viper's bite (*Vipera aspis*, *Vipera berus, Vipera ammodytes*, *Vipera ursinii*) is usually characterized by local and systemic signs, while neurological signs are infrequent and rarely described, especially in children. Neurotoxic manifestations mainly affect cranial nerves, also leading to botulinum-like symptoms. We describe two patients with neurological symptoms after *Vipera aspis* bite (both identified by an herpetologist).
Case series: Case 1. A 13-year-old boy was transferred to our emergency department about 6 hours after the bite. Fang marks were clearly visible on his left hand, with painful edema and hyperemia of the entire limb. Neurological examination revealed bilateral ptosis, diplopia and lateral nystagmus. Case 2. A 7-year-old male was admitted to our hospital 4 hours after the viper bite. On physical examination the patient presented local sign of envenomation with painful edema and hyperemia of the entire left limb, bilateral ptosis, partial ophthalmoplegia and mydriasis. Both patients were stable; however they showed leukocytosis with neutrophilia in their blood tests. According to the Grading Severity Score (GSS), both patients were classified as grade 2b and one vial of anti-viper serum (Viekvin®) was administered. Local and neurological symptoms gradually improved and the patients were discharged at day 7 and day 5, respectively.
Conclusion: Although neurotoxicity is mainly related to *Vipera ammodytes* our experience confirms the neurotoxic effect of *Vipera aspis*; nevertheless the efficacy of antisera against its neurotoxicity appears limited, and our clinical experience confirms the findings of Zanetti et al. [1] in their *in vivo* study on animal models.

Reference

[1] Zanetti G, Duregotti E, Locatelli CA, et al. Variability in venom composition of European viper subspecies limits the cross-effectiveness of antivenoms. Scientific Reports. 2018;8:9818.

Table 1. Features of cases of kambô reported to the UK NPIS.

Patient	Gender	Age	Clinical Features	Co-ingestants	Poison Severity Score (PSS)
1	M	55	Gastrointestinal upset, fever, psychosis, rhabdomyolysis, cellulitis.	No	2
2	F	Adult	Agitation, hyponatraemia.	No	2
3	M	28	Tachycardia, hypertension, respiratory arrest.	Dihydrocodeine	3
4	M	55	Chest pain, tachycardia, gastrointestinal upset.	No	1
5	M	23	Gastrointestinal upset, acute kidney injury.	Alcohol	2
6	M	35	Gastrointestinal upset, fever, tachycardia, psychosis.	No	1

292. Thromboelastogram use in *Crotalus adamanteus* envenomation

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Objective: Thromboelastography is an evolving technology to better describe coagulopathy. We previously reported on using the mean amplitude as a tool in *Crotalus horridus horridus* envenomation. Here we describe the use of LY30 (clot lysis at 30 minutes after maximum clot strength), a measure of active fibrinolysis, to guide management of severe coagulopathy from eastern diamondback (*Crotalus adamanteus*).

Case reports: Case 1. A 61-year-old female snake handler presented after being envenomated on the abdomen by her eastern diamondback during a school demonstration. Initial thromboelastogram obtained two hours post envenomation had no detectable activity which corroborated with laboratory parameters indicating systemic coagulopathy (fibrinogen <60 mg/dL; INR >11). Cumulative loading dose of 20 vials of crotalidae polyvalent immune fab was administered with eventual improvement of her fibrinogen to 81 mg/dL and a detectable LY30 of 5% (reference 1-2.9%). Recurrence of coagulopathy (INR >11; fibrinogen <60 mg/dL) occurred on admission day 2 after cessation of antivenin treatment. She was re-bolused with antivenin and resumed on maintenance therapy. Two further episodes of coagulopathy occurred over the course of 8 hospital days. Serial thromboelastograms exhibited elevated LY30 just prior to episodes of recurrence and preceded detection of hypofibrinogenemia. She was discharged on hospital day 12 without further instances of coagulopathy. Case 2. A 59-year-old male presented following envenomation to his left hand with significant swelling and edema; the snake was subsequently brought in and identified as a *Crotalus adamanteus*. All thromboelastogram values were undetectable. Other initial ancillary studies demonstrated an undetectable fibrinogen and an INR >12. He received 22 vials of antivenin over the next 26 hours before fibrinogen was detectable and LY30 improved to 3%. After 34 vials of antivenin, his fibrinogen and LY30 normalized to >100 mg/dL and zero, respectively. He had intermittent coagulopathy over the next 12 days before no longer requiring further antivenin.

Conclusion: Standard coagulation parameters are not always ideal when managing severe coagulopathy secondary to envenomation. In both cases, the thromboelastogram was unable to interpret any results and displayed a straight flat line until both victims of *Crotalus adamanteus* envenomation had been aggressively treated with antivenin. In the first case, LY30 was able to predict fibrinolysis prior to hypofibrinogenemia becoming apparent. In the second, eastern diamondback envenomation was suspected based on initial thromboelastogram pattern before visual confirmation of the snake. This guided management strategies and patient disposition. LY30 in this very limited case series was useful in identifying and managing envenomation from eastern diamondback envenomation.

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